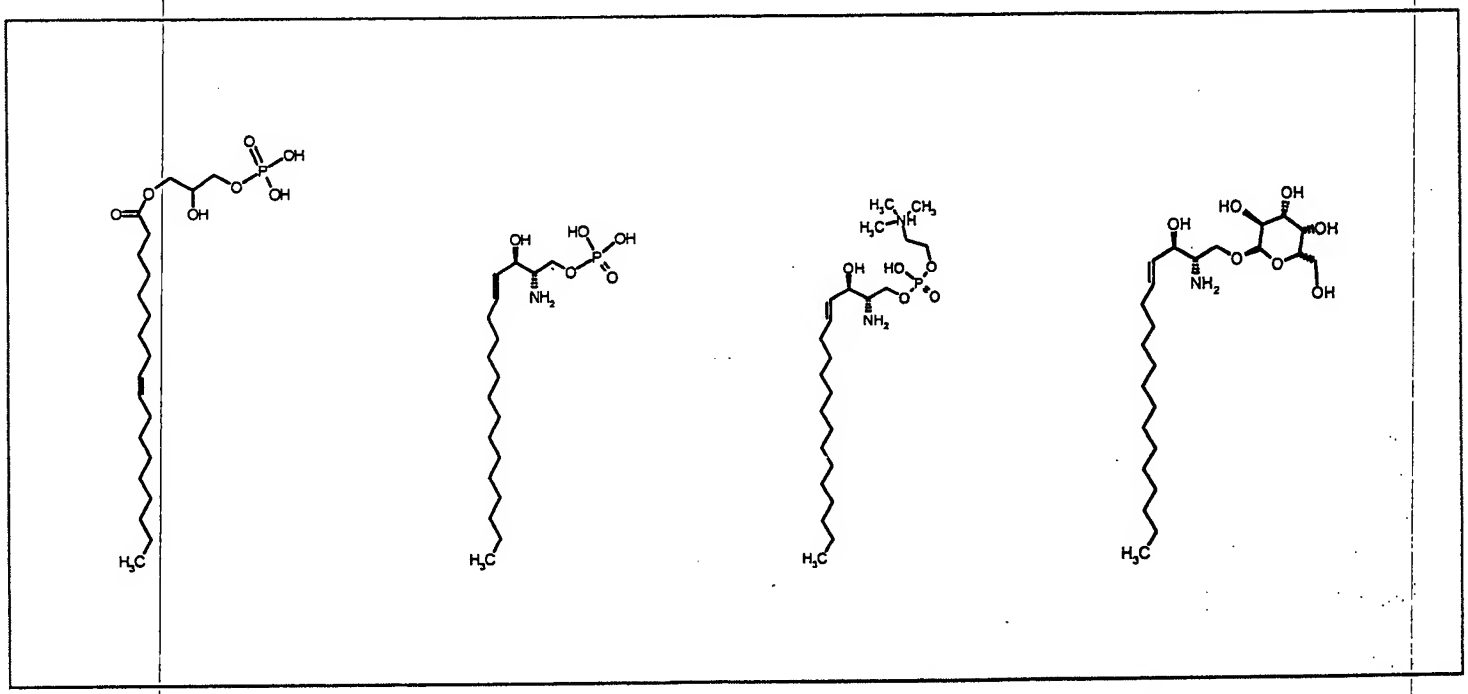
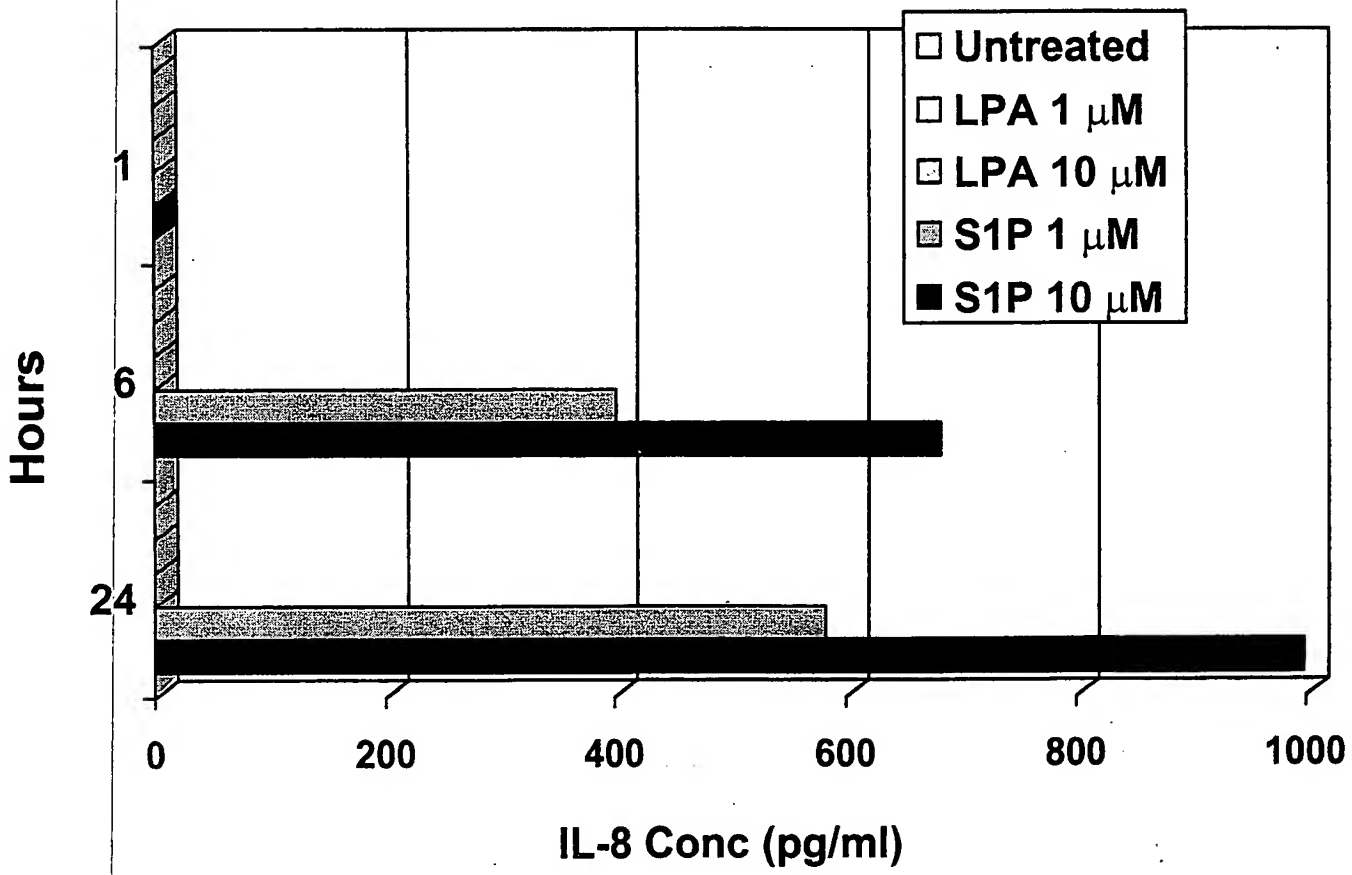
208220 "ZOSH3OOT

Figure 1A.



20820 "405t800T

Figure 1B.



208220" 705h800T

Figure 2A.

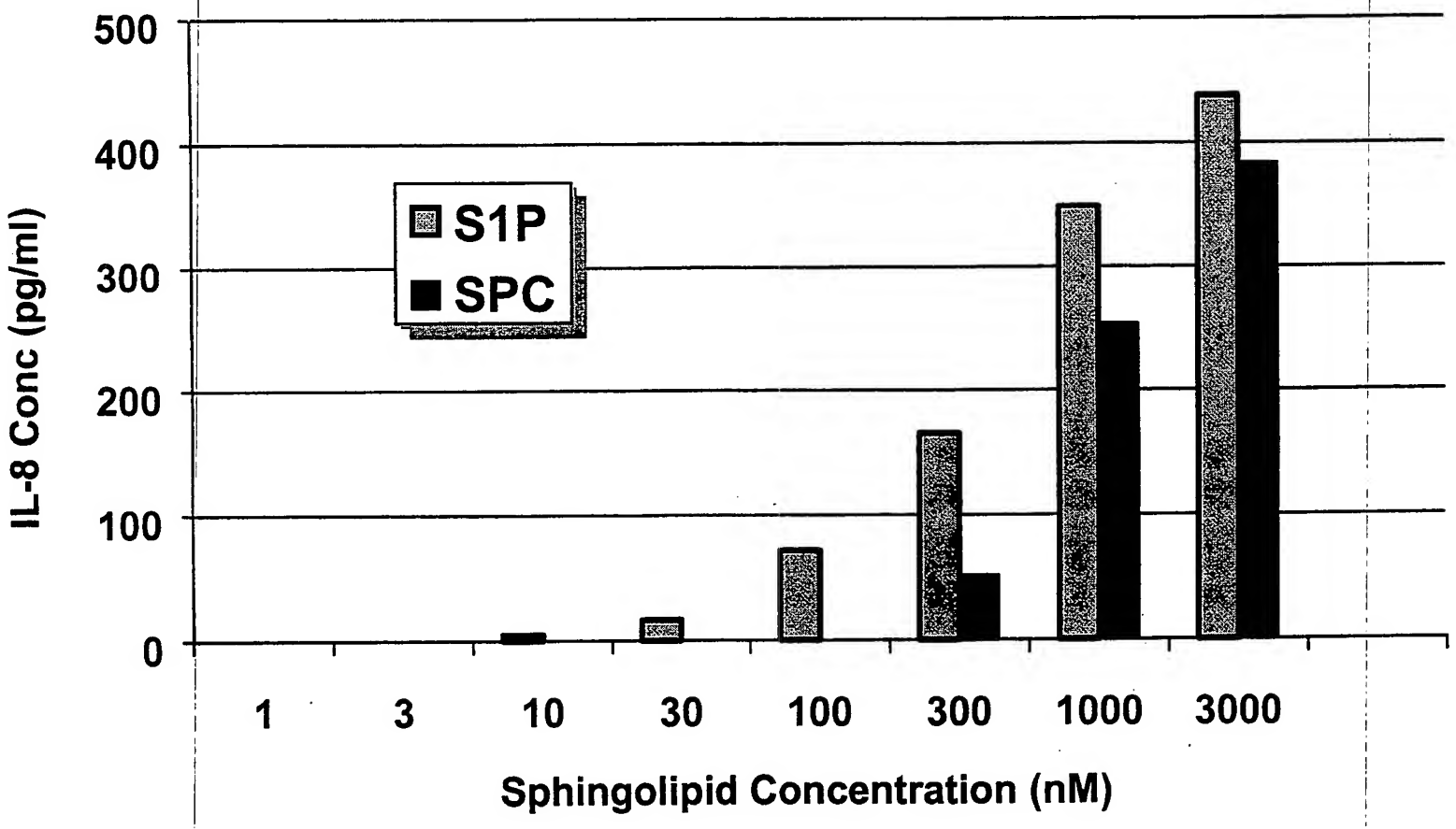
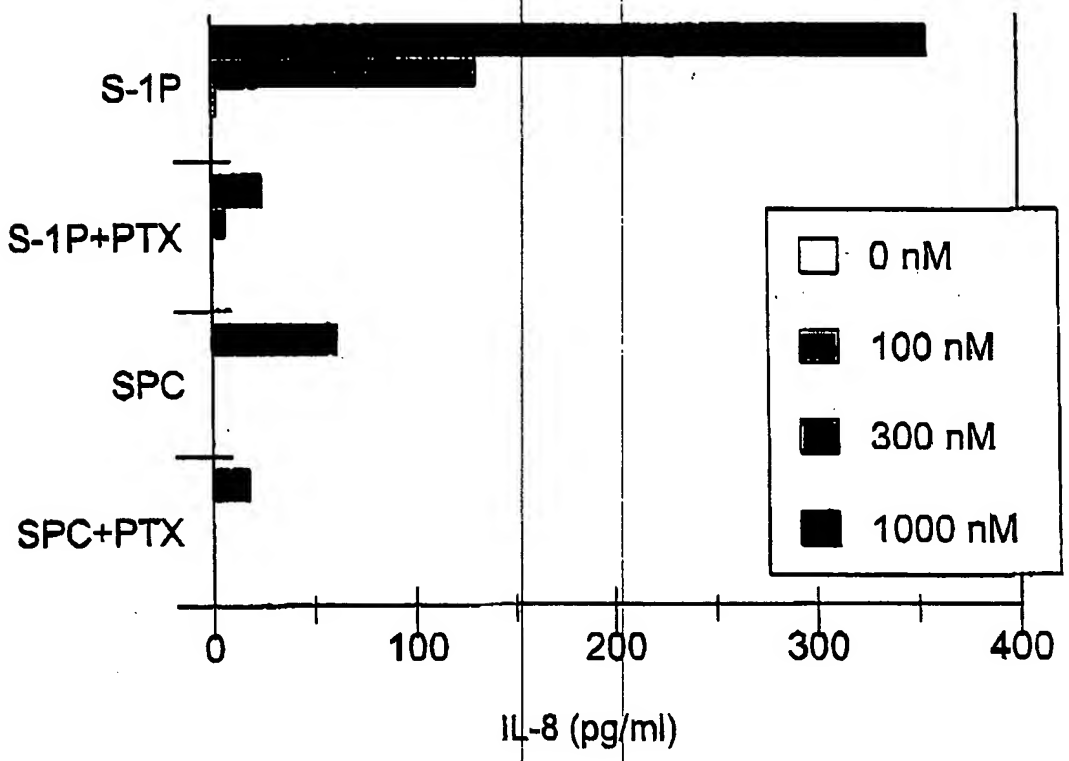


FIGURE 2


S-1P
S-1P+PTX
SPC
SPC+PTX
0 nM
100 nM
300 nM
1000 nM
0
100
200
300
400
IL-8 (pg/ml)

208220" 205h80DT

Figure 3.

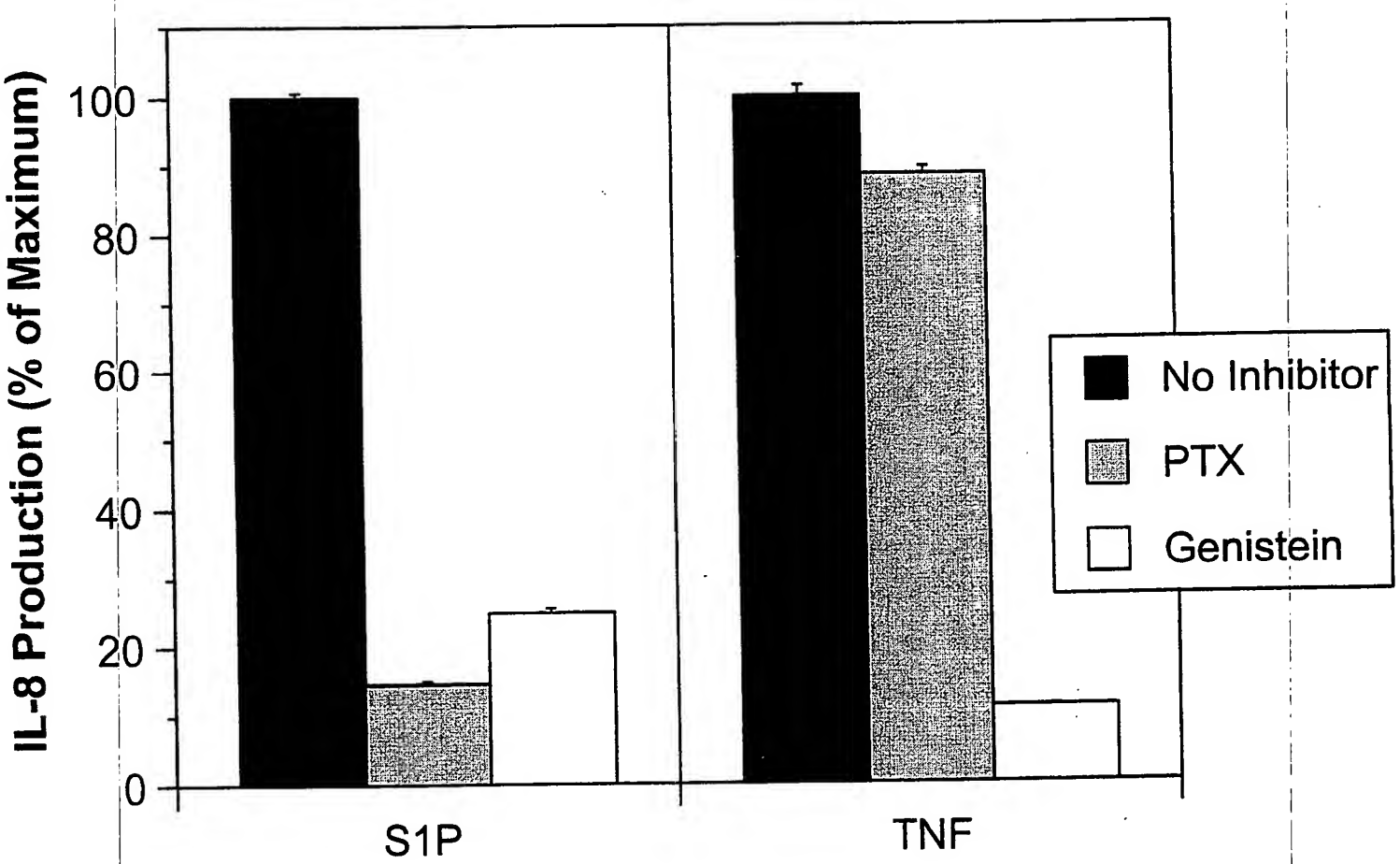
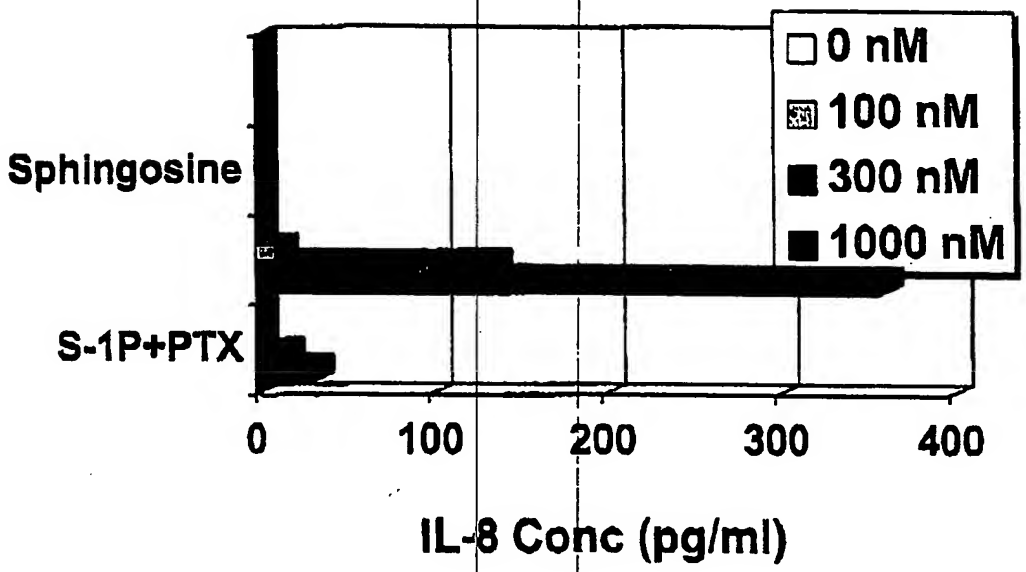
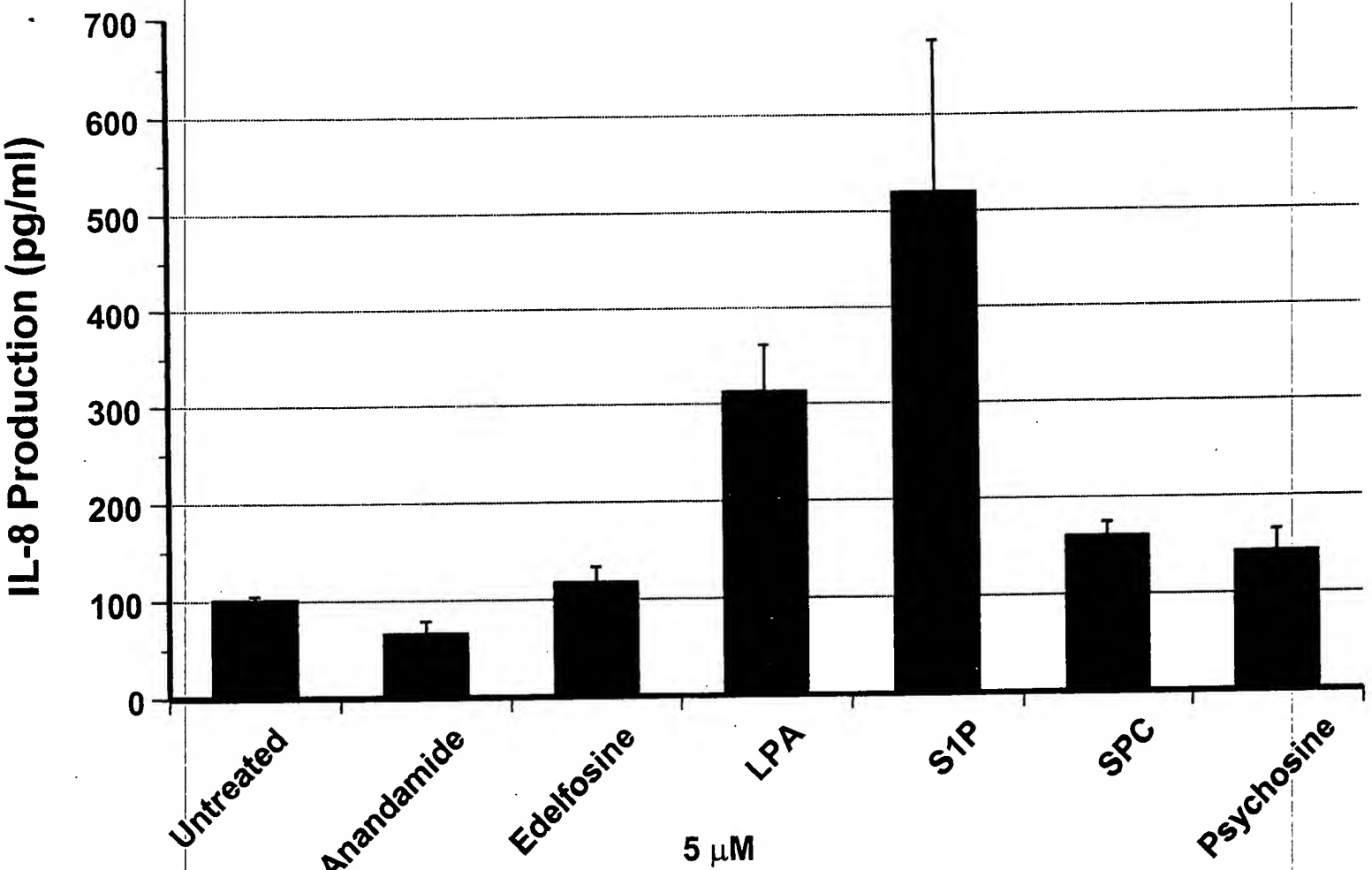


FIGURE 4A


0 nM
100 nM
300 nM
1000 nM
Sphingosine
S-1P+PTX
0
100
200
300
400
IL-8 Conc (pg/ml)

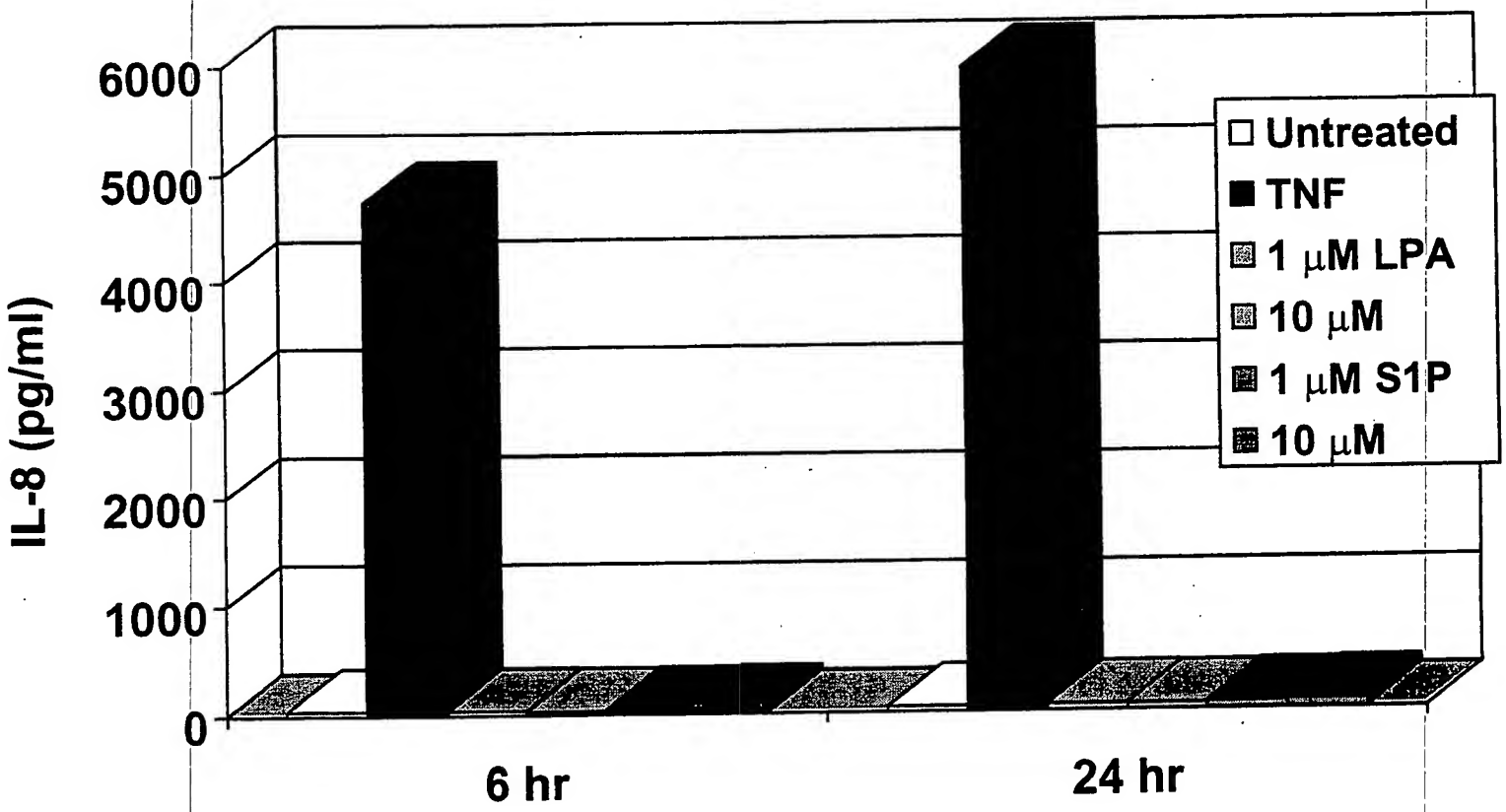
208220 20Sh800F

Figure 4B.



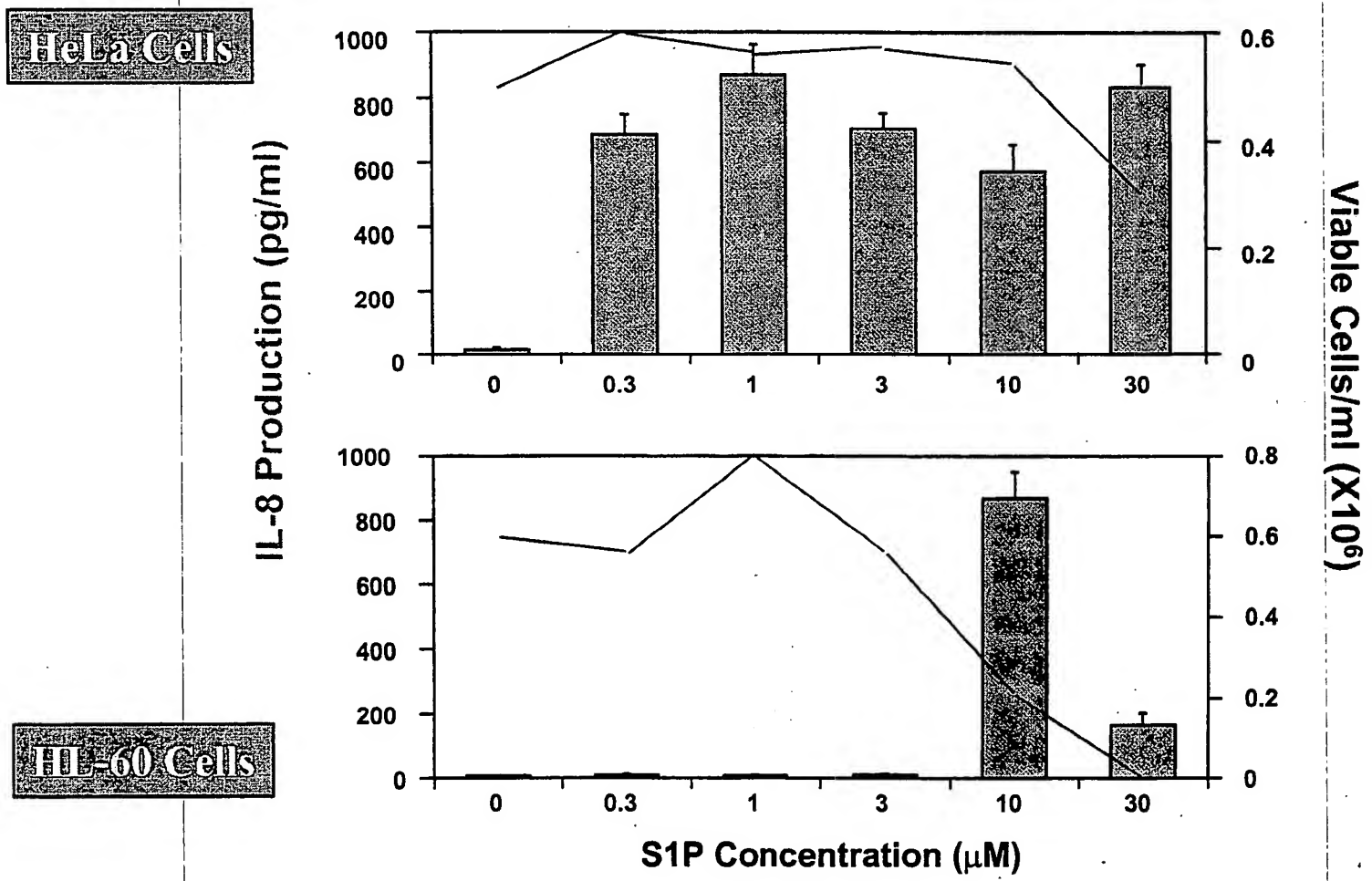
20820 "705h800T

Figure 5.



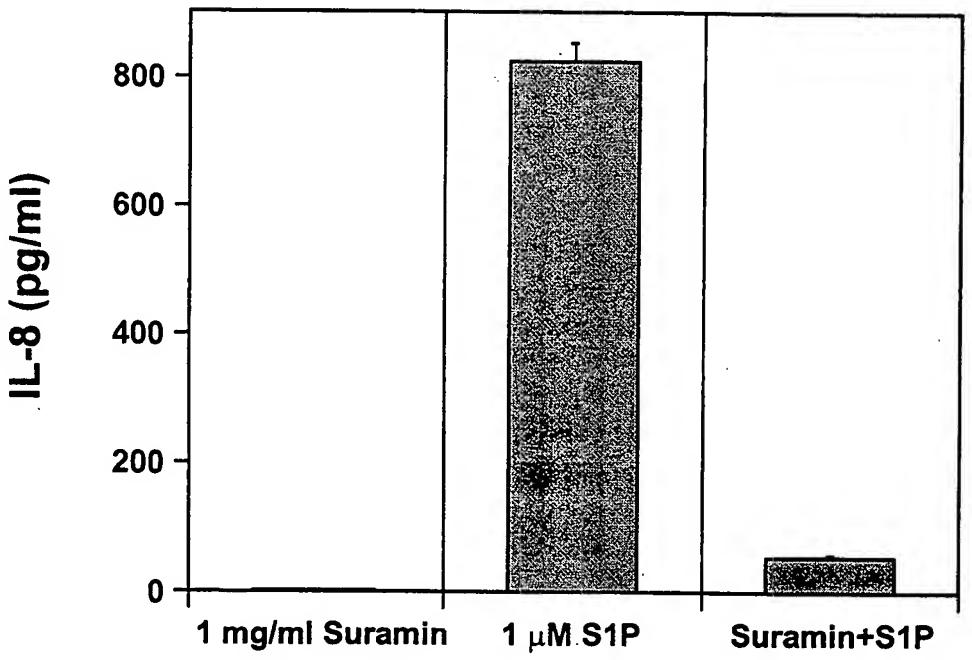
208220" 405h800T

Figure 6.



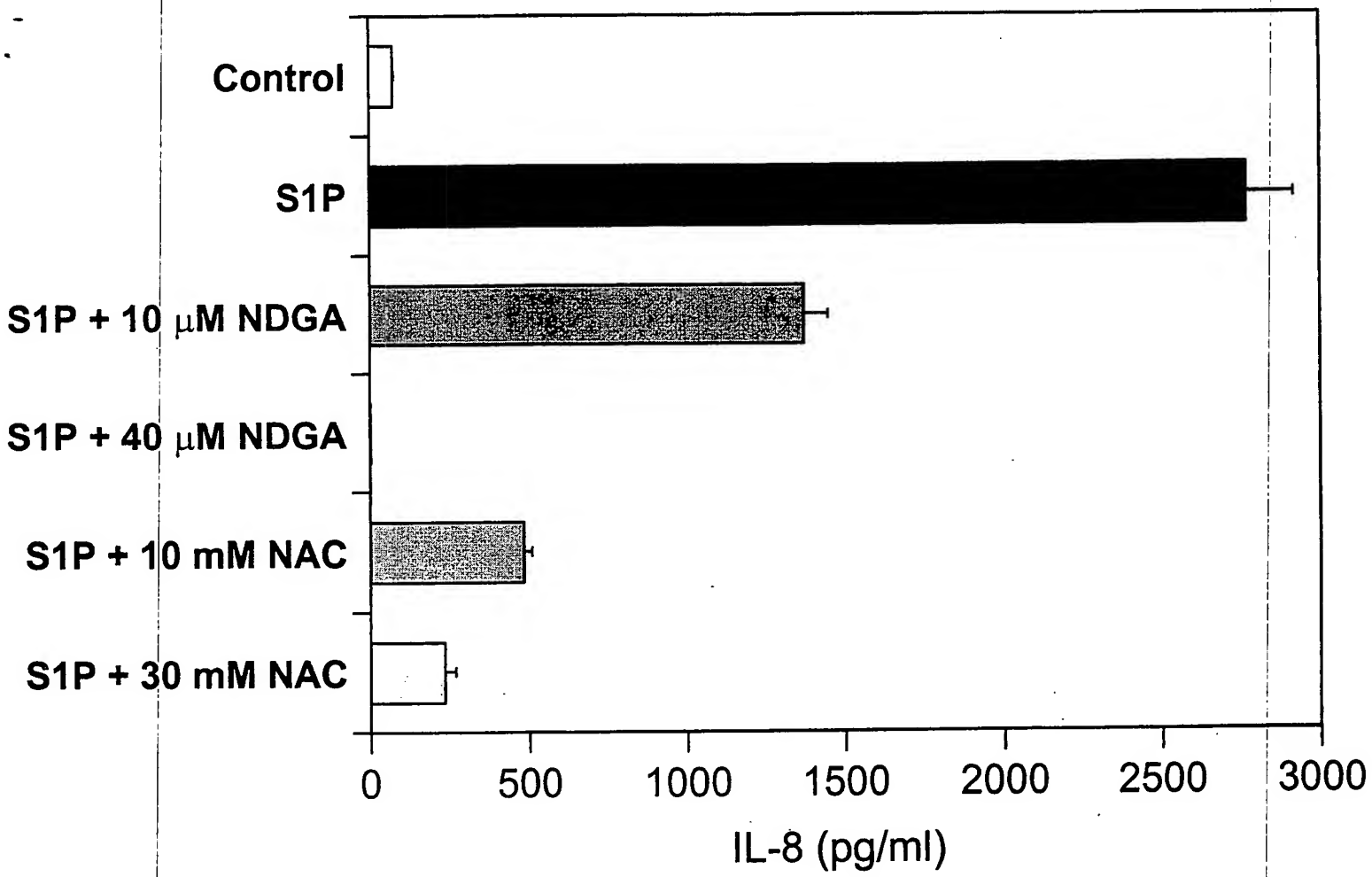
208220 "205h80T

Figure 7.



208220 '205h800T

Figure 8.



208220 "205h800T

Figure 9.

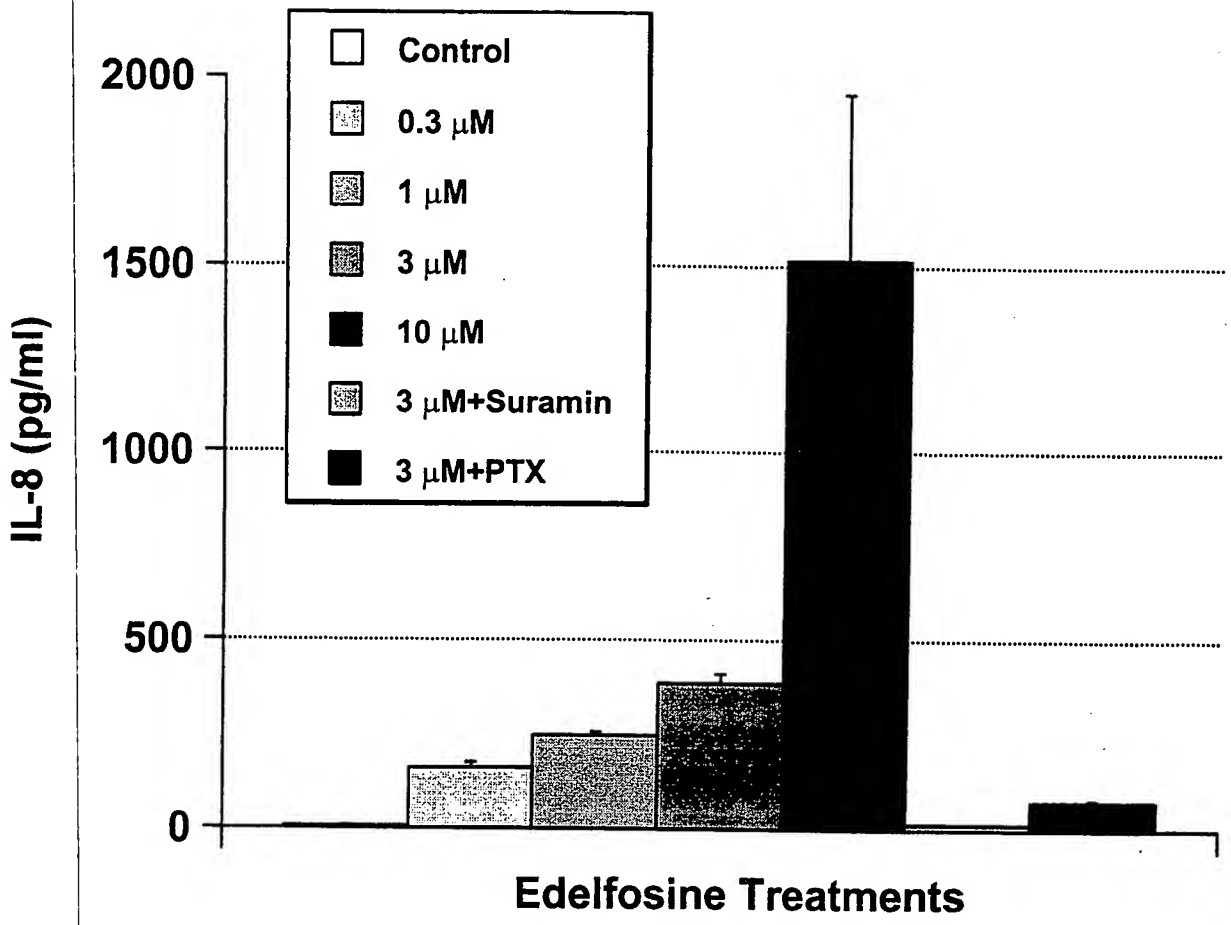
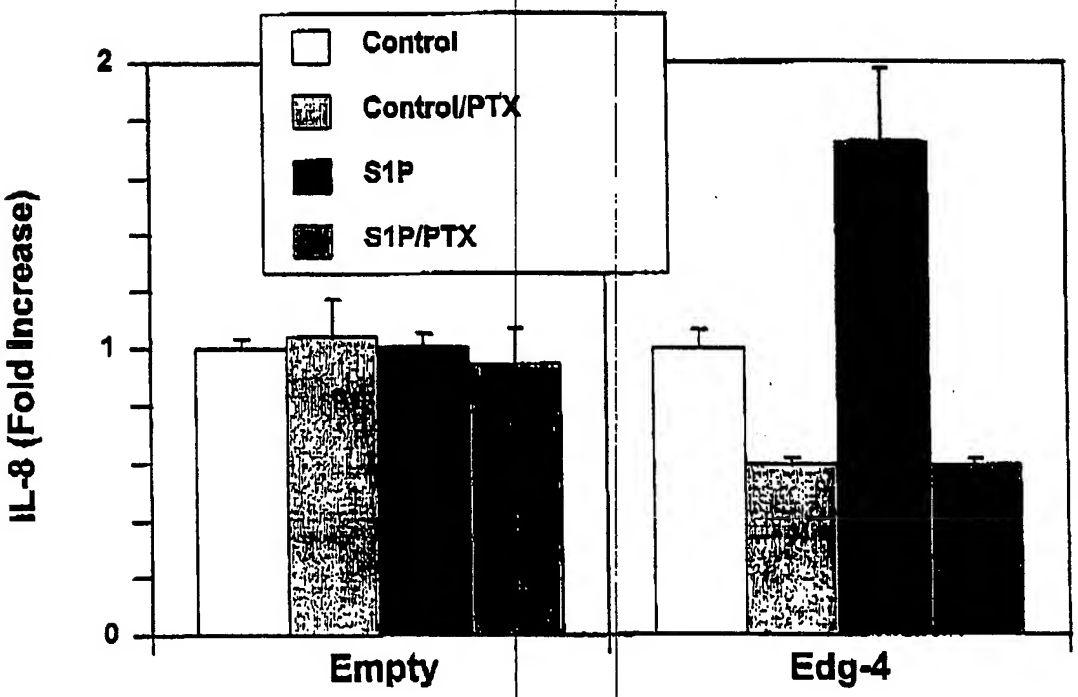
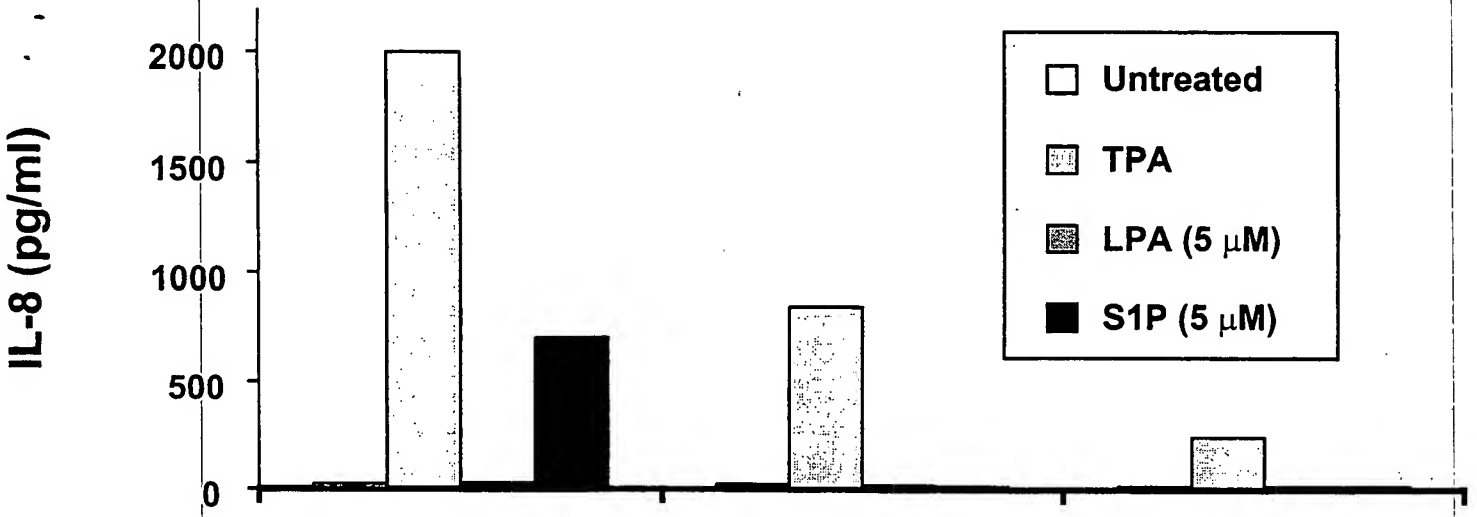


FIGURE 10A


Control
Control/PTX
S1P
S1P/PTX
IL-8 (Fold Increase)
2
1
0
Empty
Edg-4

20820 "205h800T

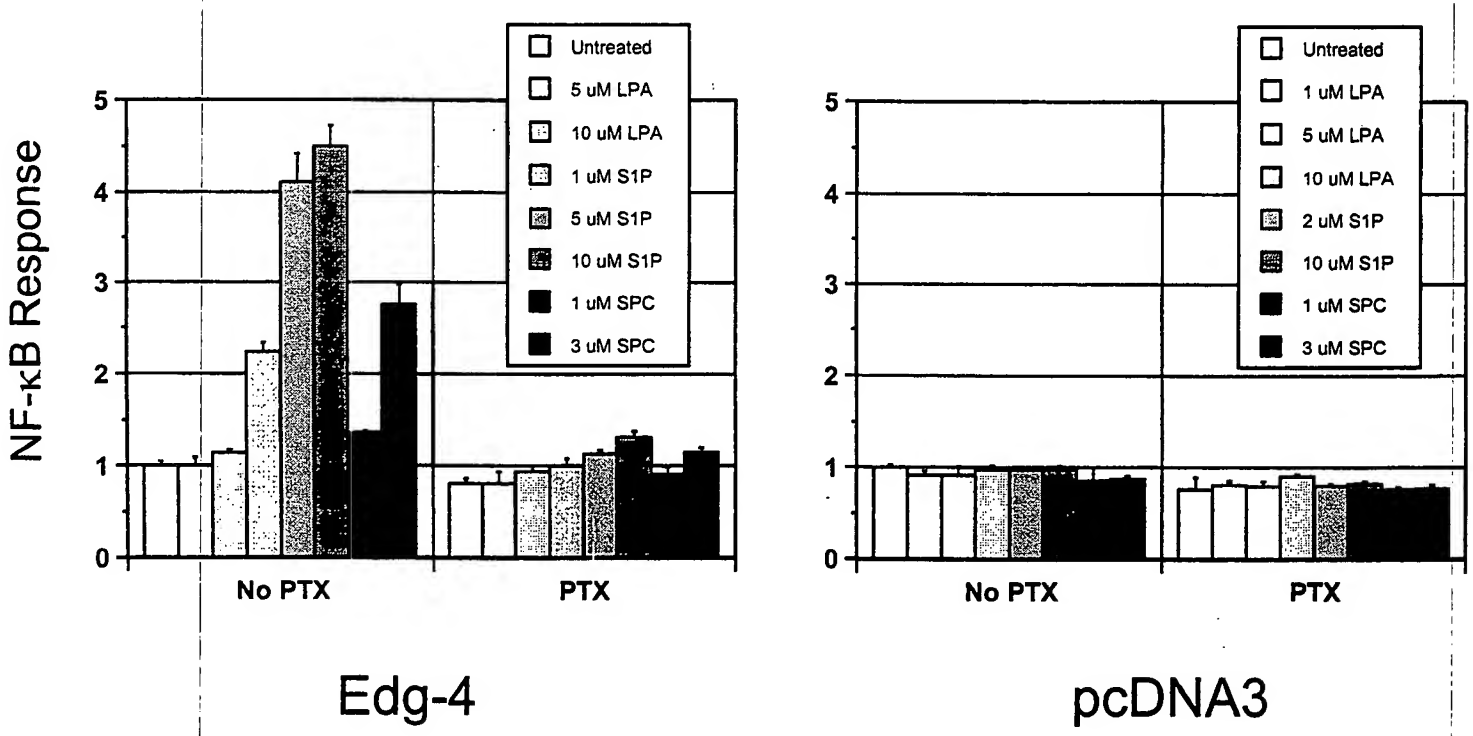
Figure 10B



Edg RNA	HeLa	COS	293-EBNA
1	+/-	+	-
2	+/-	+	-
3	++	+++	-
4	++	-	-
5	+/-	+	+
6	-	+/-	-
7	-	-	-

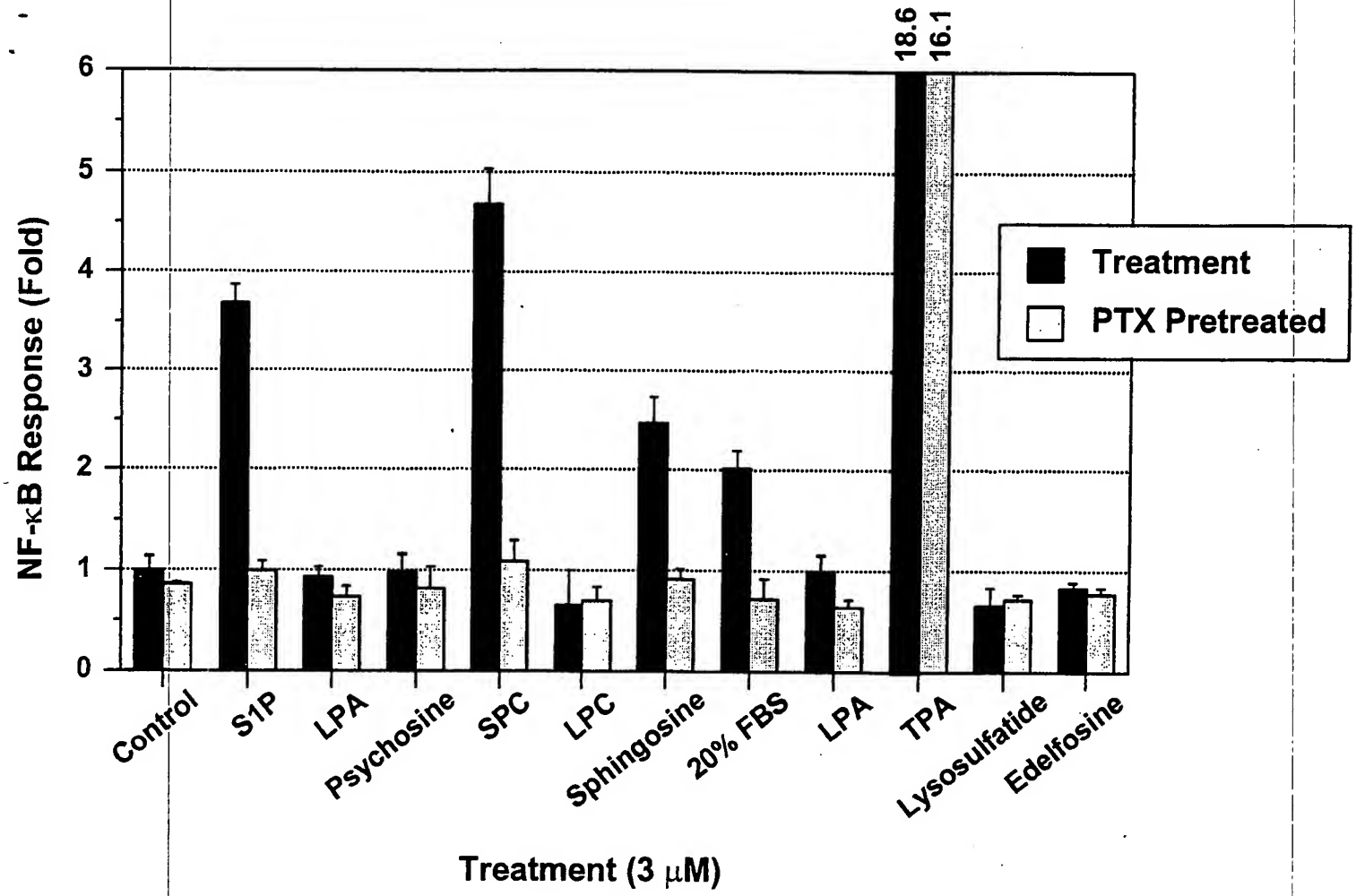
20820 205h800T

Figure 11.



208220" 205h800F

Figure 12.



208220 "405h800T

Figure 13.

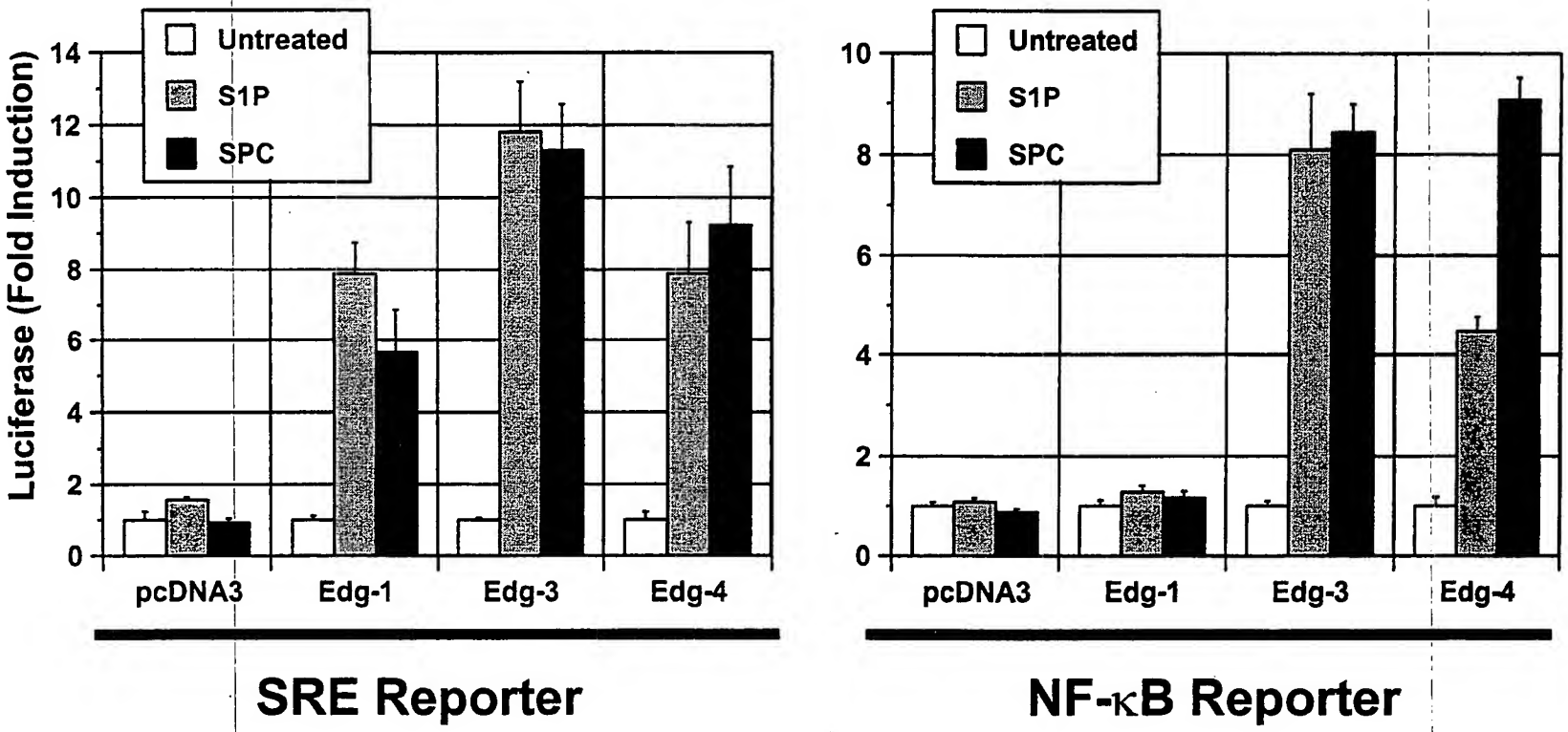
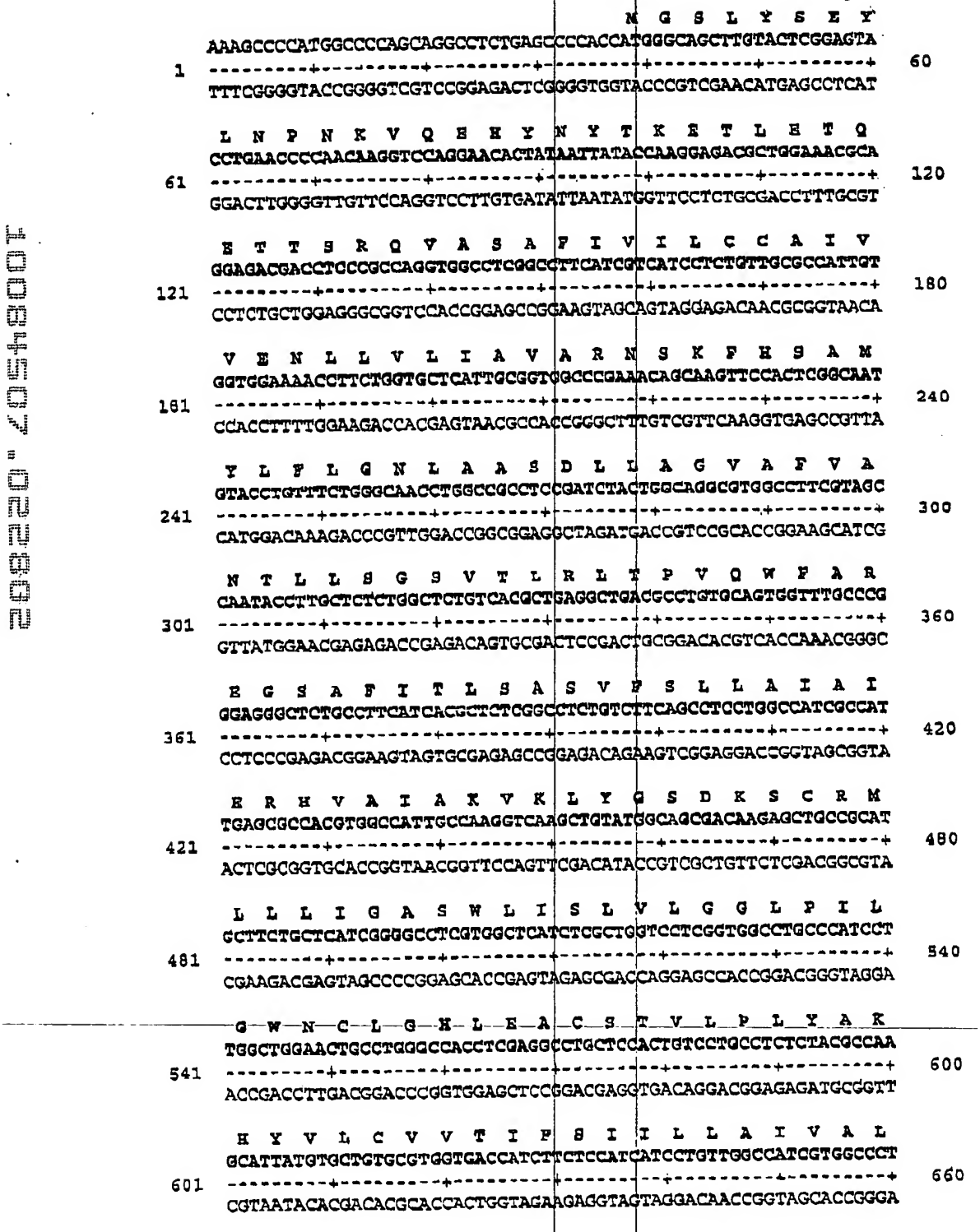


FIGURE 14

```
1                                                                50
AA834537  --------AAA GCCCCATGGC CCCAGCAGGC CTCTGAGCCC CACCATGGGC
AA804628  --------AAA GCCCCATGGC CCCAGCAGGC CTCTGAGCCC CACCATGGGC
AA827835  AGTTCTGAAA GCCCCATGGC CCCAGCAGGC CTCTGAGCCC CACCATGGGC

          51                                                    100
AA834537  AGCTTGTACT CGGAGTACCT GAACCCCAAC AAGGTCCAGG AACACTATAA
AA804628  AGCTTGTACT CGGAGTACCT GAACCCCAAC AAGGTCCAGG AACACTATAA
AA827835  AGCTTGTACT CGGAGTACCT GAACCCCAAC AAGGTCCAGG AACACTATAA

          101                                                   150
AA834537  TTATACCAAG GAGACGCTGG AAACGCAGGA GACGACCTCC CGCCAGGTGG
AA804628  TTATACCAAG GAGACGCTGG AAACGCAGGA GACGACCTCC CGCCAGGTGG
AA827835  TTATACCAAG GAGACGCTGG AAACGCAGGA GACGACCTCC CGCCAGGTGG

          151                                                   200
AA834537  CCTCGGCATT CATCGTCATC CTCTGTTGCG CCATTGTGGT GGAAAACCTT
AA804628  CCTCGGCCTT CATCGTCATC CTCTGTTGCG CCATTGTGGT GGAAAACCTT
AA827835  GCTCGGCCTT CATCGTCATC CTCTGTTGCG CCATTGTGGT GGAAAACCTT

          201                                                   250
AA834537  CTGGTGCTCA TTGCGGTGGC CCGAAACAGC AAGTTCCACT CGGCAATGTA
AA804628  CTGGTGCTCA TTGCGGTGGC CCGAAACAGC AAGTTCCACT CGGCAATGTA
AA827835  CTGGTGCTCA TTGCGGTGGC CCGAAACAGC AAGTTCCACT CGGCAATGTA

          251                                                   300
AA834537  CCTGTTTCTG GGCAACCTGG CCGCCTCCGA TCTACTGGCA GGCGTGGCCT
AA804628  CCTGTTTCTG GGCAACCTGG CCGCCTCCGA TCTACTGGCA GGCGTGGCCT
AA827835  CCTGTTTCTG GGCAACCTGG CCGCCTCCGA TCTACTGGCA GGCGTGG.CT

          301                                                   350
AA834537  TCGTAGCCAA TACCTTGCTC TCTGGCTCTG TCACGCTGAG GCTGACGCCT
AA804628  TCGTAGCCAA TACCTTGCTC TCTGGCTCTG TCACGCTGAG GCTGACGCCT
AA827835  TCGTAGCCAA TACCTTGCTC TCTGGCTCTG TCACGCTGAG GCTGACGCCT

          351                                                   400
AA834537  GTGCAGTGGT TTGCCCGGGA CGGTCTGCCT TCATCACGCT CTCGGCCTCT
AA804628  GTGCAGTGGT TTGCCCGGGA C---------- ---------- ----------
AA827835  GTGCAGTGGT TTGCCCGGGA ---------- ---------- ----------

          401                                                   450
AA834537  GTCTTCAGCC TCCTGGCCAT CGCCATTGAG CGCCACGTGG CCATTGCAAA
AA804628  ---------- ---------- ---------- ---------- ----------
AA827835  ---------- ---------- ---------- ---------- ----------

          451
AA834537  GG
AA804628  --
AA827835  --
```

20030203.7054800

FIGURE 15 A


M G S L Y S E Y
AAAGCCCCATGGCCCCAGCAGGCCTCTGAGCCCCACCATGGGCAGCTTGTACTCGGAGTA
1 60
TTTCGGGGTACCGGGGTCGTCCGGAGACTCGGGGTGGTACCCGTCGAACATGAGCCTCAT
L N P N K V Q E H Y N Y T K E T L E T Q
CCTGAACCCCAACAAGGTCCAGGAACACTATAATTATACCAAGGAGACGCTGGAAACGCA
61 120
GGACTTGGGGTTGTTCCAGGTCCTTGTGATATTAATATGGTTCCTCTGCGACCTTTGCGT
E T T S R Q V A S A F I V I L C C A I V
GGAGACGACCTCCCGCCAGGTGGCCTCGGCGTTCATCGTCATCCTCTGTTGCGCCATTGT
121 180
CCTCTGCTGGAGGGCGGTCCACCGGAGCCGGAAGTAGCAGTAGGAGACAACGCGGTAACA
V E N L L V L I A V A R N S K F H S A M
GGTGGAAAACCTTCTGGTGCTCATTGCGGTGGCCCGAAACAGCAAGTTCCACTCGGCAAT
181 240
CCACCTTTTGGAAGACCACGAGTAACGCCACCGGGCTTTGTCGTTCAAGGTGAGCCGTTA
Y L F L G N L A A S D L L A G V A F V A
GTACCTGTTTCTGGGCAACCTGGCCGCCTCCGATCTACTGGCAGGCGTGGCCTTCGTAGC
241 300
CATGGACAAAGACCCGTTGGACCGGCGGAGGCTAGATGACCGTCCGCACCGGAAGCATCG
N T L L S G S V T L R L T P V Q W F A R
CAATACCTTGCTCTCTGGCTCTGTCACGCTGAGGCTGACGCCTGTGCAGTGGTTTGCCCG
301 360
GTTATGGAACGAGAGACCGAGACAGTGCGACTCCGACTGCGGACACGTCACCAAACGGGC
E G S A F I T L S A S V F S L L A I A I
GGAGGGCTCTGCCTTCATCACGCTCTCGGCCTCTGTCTTCAGCCTCCTGGCCATCGCCAT
361 420
CCTCCCGAGACGGAAGTAGTGCGAGAGCCGGAGACAGAAGTCGGAGGACCGGTAGCGGTA
E R H V A I A K V K L Y G S D K S C R M
TGAGCGCCACGTGGCCATTGCCAAGGTCAAGCTGTATGGCAGCGACAAGAGCTGCCGCAT
421 480
ACTCGCGGTGCACCGGTAACGGTTCCAGTTCGACATACCGTCGCTGTTCTCGACGGCGTA
L L L I G A S W L I S L V L G G L P I L
GCTTCTGCTCATCGGGGCCTCGTGGCTCATCTCGCTGGTCCTCGGTGGCCTGCCCATCCT
481 540
CGAAGACGAGTAGCCCCGGAGCACCGAGTAGAGCGACCAGGAGCCACCGGACGGGTAGGA
G W N C L G H L E A C S T V L P L Y A K
TGGCTGGAACTGCCTGGGCCACCTCGAGGCCTGCTCCACTGTCCTGCCTCTCTACGCCAA
541 600
ACCGACCTTGACGGACCCGGTGGAGCTCCGGACGAGGTGACAGGACGGAGAGATGCGGTT
H Y V L C V V T I P S I I L L A I V A L
GCATTATGTGCTGTGCGTGGTGACCATCTTCTCCATCATCCTGTTGGCCATCGTGGCCCT
601 660
CGTAATACACGACACGCACCACTGGTAGAAGAGGTAGTAGGACAACCGGTAGCACCGGGA

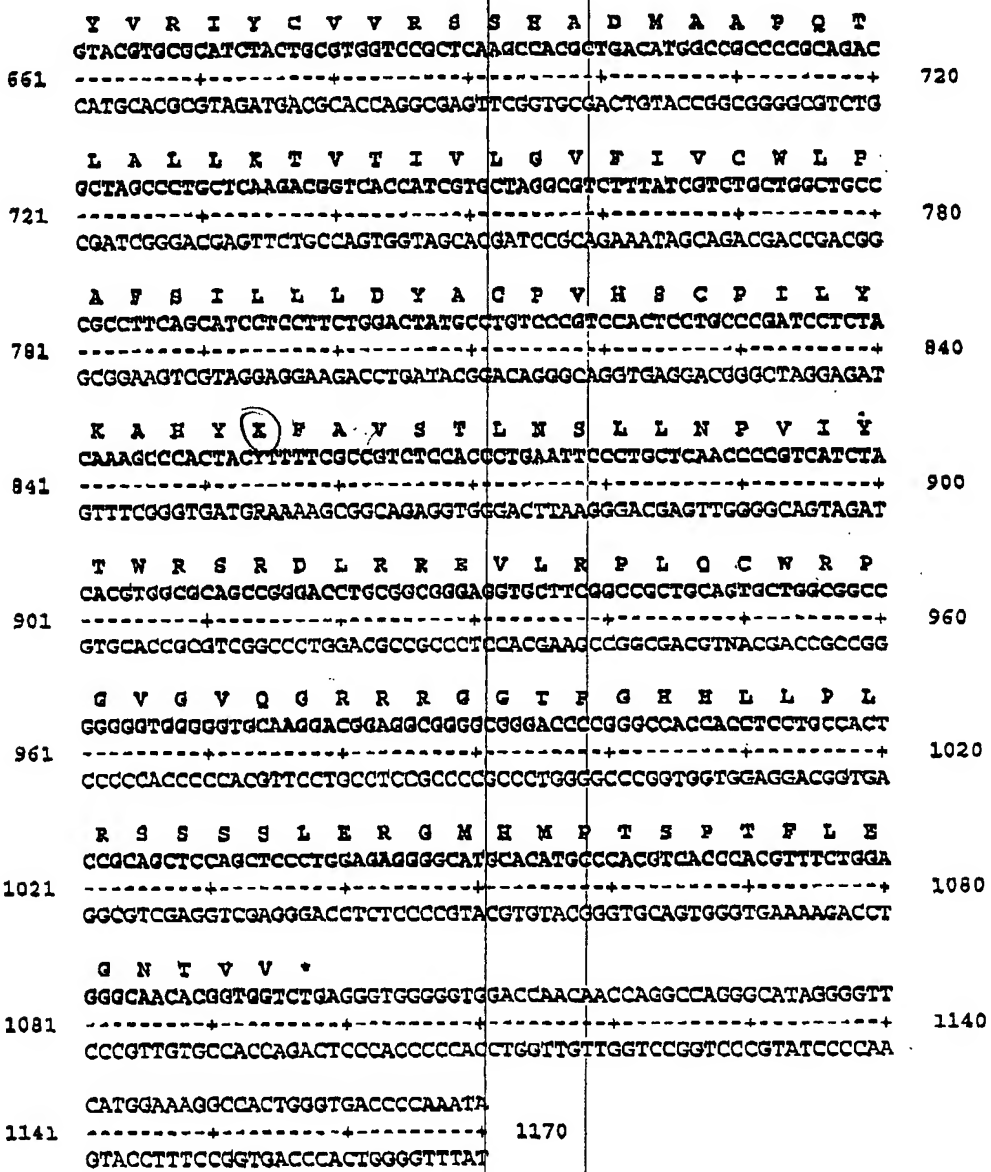

Y V R I Y C V V R S S E A D M A A P Q T
GTACGTGCGCATCTACTGCGTGGTCCGCTCAAGCCACGCTGACATGGCCGCCCCGCAGAC
661
720
CATGCACGCGTAGATGACGCACCAGGCGAGTTCGGTGCGACTGTACCGGCGGGGCGTCTG
L A L L K T V T I V L G V F I V C W L P
GCTAGCCCTGCTCAAGACGGTCACCATCGTGCTAGGCGTCTTTATCGTCTGCTGGCTGCC
721
780
CGATCGGGACGAGTTCTGCCAGTGGTAGCACGATCCGCAGAAATAGCAGACGACCGACGG
A F S I L L L D Y A C P V H S C P I L Y
CGCCTTCAGCATCCTCCTTCTGGACTATGCCTGTCCCGTCCACTCCTGCCCGATCCTCTA
781
840
GCGGAAGTCGTAGGAGGAAGACCTGATACGGACAGGGCAGGTGAGGACGGGCTAGGAGAT
K A H Y X F A V S T L N S L L N P V I Y
CAAAGCCCACTACTTTTTCGCCGTCTCCACCCTGAATTCCCTGCTCAACCCCGTCATCTA
841
900
GTTTCGGGTGATGRAAAAGCGGCAGAGGTGGGACTTAAGGGACGAGTTGGGGCAGTAGAT
T W R S R D L R R E V L R P L Q C W R P
CACGTGGCGCAGCCGGGACCTGCGGCGGGAGGTGCTTCGGCCGCTGCAGTGCTGGCGGCC
901
960
GTGCACCGCGTCGGCCCTGGACGCCGCCCTCCACGAAGCCGGCGACGTNACGACCGCCGG
G V G V Q G R R R G G T P G H H L L P L
GGGGGTGGGGGTGCAAGGACGGAGGCGGGGCGGGACCCCGGGCCACCACCTCCTGCCACT
961
1020
CCCCCACCCCCACGTTCCTGCCTCCGCCCCGCCCTGGGGCCCGGTGGTGGAGGACGGTGA
R S S S S L E R G M H M P T S P T F L E
CCGCAGCTCCAGCTCCCTGGAGAGGGGCATGCACATGCCCACGTCACCCACGTTTCTGGA
1021
1080
GGCGTCGAGGTCGAGGGACCTCTCCCCGTACGTGTACGGGTGCAGTGGGTGAAAAGACCT
G N T V V *
GGGCAACACGGTGGTCTGAGGGTGGGGGTGGACCAACAACCAGGCCAGGGCATAGGGGTT
1081
1140
CCCGTTGTGCCACCAGACTCCCACCCCCACCTGGTTGTTGGTCCGGTCCCGTATCCCCAA
CATGGAAAGGCCACTGGGTGACCCCAAATA
1141
1170
GTACCTTTCCGGTGACCCACTGGGGTTTAT

Figure 15B

cDNA sequence of clone pC3-hedg4#36 encoding functional HEDG4 receptor protein.

```
      ATGGGCAGCTTGTACTCGGAGTACCTGAACCCCAACAAGGTCCAGGAACACTATAATTAT
    1 ---------+---------+---------+---------+---------+---------+   60
      TACCCGTCGAACATGAGCCTCATGGACTTGGGGTTGTTCCAGGTCCTTGTGATATTAATA

      ACCAAGGAGACGCTGGAAACGCAGGAGACGACCTCCCGCCAGGTGGCCTCGGCCTTCATC
   61 ---------+---------+---------+---------+---------+---------+  120
      TGGTTCCTCTGCGACCTTTGCGTCCTCTGCTGGAGGGCGGTCCACCGGAGCCGGAAGTAG

      GTCATCCTCTGTTGCGCCATTGTGGTGGAAAACCTTCTGGTGCTCATTGCGGTGGCCCGA
  121 ---------+---------+---------+---------+---------+---------+  180
      CAGTAGGAGACAACGCGGTAACACCACCTTTTGGAAGACCACGAGTAACGCCACCGGGCT

      AACAGCAAGTTCCACTCGGCAATGTACCTGTTTCTGGGCAACCTGGCCGCCTCCGATCTA
  181 ---------+---------+---------+---------+---------+---------+  240
      TTGTCGTTCAAGGTGAGCCGTTACATGGACAAAGACCCGTTGGACCGGCGGAGGCTAGAT

      CTGGCAGGCGTGGCCTTCGTAGCCAATACCTTGCTCTCTGGCTCTGTCACGCTGAGGCTG
  241 ---------+---------+---------+---------+---------+---------+  300
      GACCGTCCGCACCGGAAGCATCGGTTATGGAACGAGAGACCGAGACAGTGCGACTCCGAC

      ACGCCTGTGCAGTGGTTTGCCCGGGAGGGCTCTGCCTTCATCACGCTCTCGGCCTCTGTC
  301 ---------+---------+---------+---------+---------+---------+  360
      TGCGGACACGTCACCAAACGGGCCCTCCCGAGACGGAAGTAGTGCGAGAGCCGGAGACAG

      TTCAGCCTCCTGGCCATCGCCATTGAGCGCCACGTGGCCATTGCCAAGGTCAAGCTGTAT
  361 ---------+---------+---------+---------+---------+---------+  420
      AAGTCGGAGGACCGGTAGCGGTAACTCGCGGTGCACCGGTAACGGTTCCAGTTCGACATA

      GGCAGCGACAAGAGCTGCCGCATGCTTCTGCTCATCGGGGCCTCGTGGCTCATCTCGCTG
  421 ---------+---------+---------+---------+---------+---------+  480
      CCGTCGCTGTTCTCGACGGCGTACGAAGACGAGTAGCCCCGGAGCACCGAGTAGAGCGAC

      GTCCTCGGTGGCCTGCCCATCCTTGGCTGGAACTGCCTGGGCCACCTCGAGGCCTGCTCC
  481 ---------+---------+---------+---------+---------+---------+  540
      CAGGAGCCACCGGACGGGTAGGAACCGACCTTGACGGACCCGGTGGAGCTCCGGACGAGG

      ACTGTCCTGCCTCTCTACGCCAAGCATTATGTGCTGTGCGTGGTGACCATCTTCTCCATC
  541 ---------+---------+---------+---------+---------+---------+  600
      TGACAGGACGGAGAGATGCGGTTCGTAATACACGACACGCACCACTGGTAGAAGAGGTAG

      ATCCTGTTGGCCGTCGTGGCCCTGTACGTGCGCATCTACTGCGTGGTCCGCTCAAGCCAC
  601 ---------+---------+---------+---------+---------+---------+  660
      TAGGACAACCGGCAGCACCGGGACATGCACGCGTAGATGACGCACCAGGCGAGTTCGGTG

      GCTGACATGGCCGCCCCGCAGACGCTAGCCCTGCTCAAGACGGTCACCATCGTGCTAGGC
  661 ---------+---------+---------+---------+---------+---------+  720
      CGACTGTACCGGCGGGGCGTCTGCGATCGGGACGAGTTCTGCCAGTGGTAGCACGATCCG

      GTCTTTATCGTCTGCTGGCTGCCCGCCTTCAGCATCCTCCTTCTGGACTATGCCTGTCCC
  721 ---------+---------+---------+---------+---------+---------+  780
```

09/09/2005 10:55 FAX 202 659 9076

4,908,305

```
      CAGAAATAGCAGACGACCGACGGGCGGAAGTCGTAGGAGGAAGACCTGATACGGACAGGG

      GTCCACTCCTGCCCGATCCTCTACAAAGCCCACTACCTTTTCGCCGTCTCCACCCTGAAT
781   ---------+---------+---------+---------+---------+---------+   840
      CAGGTGAGGACGGGCTAGGAGATGTTTCGGGTGATGGAAAAGCGGCAGAGGTGGGACTTA

      TCCCTGCTCAACCCCGTCATCTACACGTGGCGCAGCCGGGACCTGCGGCGGGAGGTGCTT
841   ---------+---------+---------+---------+---------+---------+   900
      AGGGACGAGTTGGGGCAGTAGATGTGCACCGCGTCGGCCCTGGACGCCGCCCTCCACGAA

      CGGCCGCTGCAGTGCTGGCGGCCGGGGGTGGGGGTGCAAGGACGGAGGCGGGGCGGGACC
901   ---------+---------+---------+---------+---------+---------+   960
      GCCGGCGACGTCACGACCGCCGGCCCCCACCCCCACGTTCCTGCCTCCGCCCCGCCCTGG

      CCGGGCCACCACCTCCTGCCACTCCGCAGCTCCAGCTCCCTGGAGAGGGGCATGCACATG
961   ---------+---------+---------+---------+---------+---------+  1020
      GGCCCGGTGGTGGAGGACGGTGAGGCGTCGAGGTCGAGGGACCTCTCCCCGTACGTGTAC

      CCCACGTCACCCACGTTTCTGGAGGGCAACACGGTGGTCTGA
1021  ---------+---------+---------+---------+--  1062
      GGGTGCAGTGGGTGCAAAGACCTCCCGTTGTGCCACCAGACT
```

FIGURE 16 A

```
  1  MGSLYSEYLN PNKVQEHYNY TKETLSTQET TSRQVASAFI VILCCAIVVE

 51  NLLVLIAVAR NSKFHSAMYL FLGNLAASDL LAGVAFVANT LLSGSVTLRL

101  TPVQWFAREG SAFITLSASV FSLLAIAIER HVAIAKVKLY GSDKSCRMLL

151  LIGASWLISL VLGGLPILGW NCLGHLEACS TVLPLYAKHY VLCVVTIFSI

201  ILLAIVALYV RIYCVVRSSH ADMAAPQTLA LLKTVTIVLG VFIVCWLPAF

251  SILLLDYACP VHSCPILYKA HYFAVSTLN SLLNPVIYTW RSRDLRREVL

301  RPLQCWRPGV GVQGRRRGGT PGHHLLPLRS SSSLERGMHM PTSPTFLEGN

351  TVV*
```

Conserved features of G-protein coupled receptors include:

N-terminal extracellular domain:	Residues 1 - 36
TM-I:	Residues 37 - 57
Intracellular loop 1:	Residues 58 - 68
TM-II:	Residues 69 - 92
Extracellular loop 1:	Residues 93 - 111
TM-III:	Residues 112 - 130
Intracellular loop 2:	Residues 131 - 149
TM-IV:	Residues 150 - 168
Extracellular loop 2:	Residues 169 - 185
TM-V:	Residues 186 - 210
Intracellular loop 3:	Residues 211 - 232
TM-VI:	Residues 233 - 254
Extracellular loop 3:	Residues 255 - 266
TM-VII:	Residues 267 - 285
C-terminal cytoplasmic domain:	Residues 286 - 353

Potential post-transcriptional modification sites:

N-glycosylation:	Residues 19
Phosphorylation:	Residues 142, 145, 219, 289,332, 345
Myristylation:	Residues 141, 318

WO 98/05769 PCT/US97/13807

Figure 16B

Predicted amino acid sequence of HEDG4 polypeptide encoded by pC3-hedg4#36.

```
   1  MGSLYSEYLN PNKVQEHYNY TKETLETQET TSRQVASAFI VILCCAIVVE

  51  NLLVLIAVAR NSKFHSAMYL FLGNLAASDL LAGVAFVANT LLSGSVTLRL

 101  TPVQWFAREG SAFITLSASV FSLLAIAIER HVAIAKVKLY GSDKSCRMLL

 151  LIGASWLISL VLGGLPILGW NCLGHLEACS TVLPLYAKHY VLCVVTIFSI

 201  ILLAVVALYV RIYCVVRSSH ADMAAPQTLA LLKTVTIVLG VFIVCWLPAF

 251  SILLLDYACP VHSCPILYKA HYLFAVSTLN SLLNPVIYTW RSRDLRREVL

 301  RPLQCWRPGV GVQGRRRGGT PGHHLLPLRS SSSLERGMHM PTSPTFLEGN

 351  TVV
```

FIGURE 17A

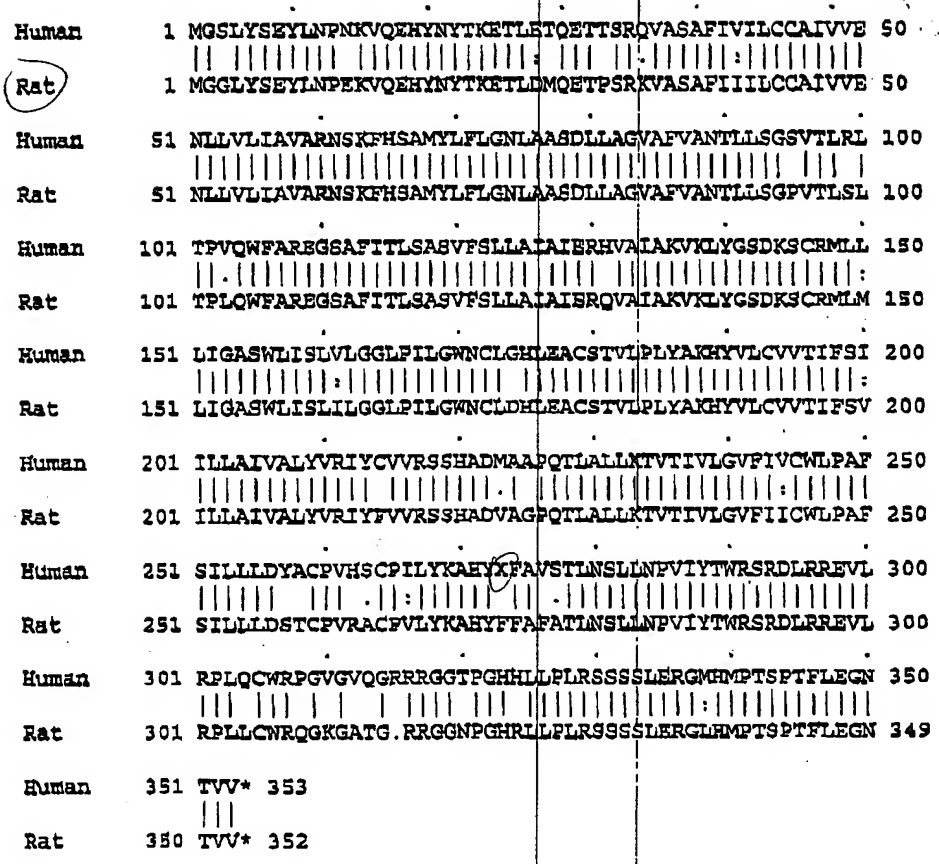

Human 1 MGSLYSEYLNPNKVQEHYNYTKETLETQETTSRQVASAFIVILCCAIVVE 50
Rat 1 MGGLYSEYLNPEKVQEHYNYTKETLDMQETPSRKVASAFIIILCCAIVVE 50
Human 51 NLLVLIAVARNSKFHSAMYLFLGNLAASDLLAGVAFVANTLLSGSVTLRL 100
Rat 51 NLLVLIAVARNSKFHSAMYLFLGNLAASDLLAGVAFVANTLLSGPVTLSL 100
Human 101 TPVQWFAREGSAFITLSASVFSLLAIAIERHVAIAKVKLYGSDKSCRMLL 150
Rat 101 TPLQWFAREGSAFITLSASVFSLLAIAIERQVAIAKVKLYGSDKSCRMLM 150
Human 151 LIGASWLISLVLGGLPILGWNCLGHLEACSTVLPLYAKHYVLCVVTIFSI 200
Rat 151 LIGASWLISLILGGLPILGWNCLDHLEACSTVLPLYAKHYVLCVVTIFSV 200
Human 201 ILLAIVALYVRIYCVVRSSHADMAAPQTLALLKTVTIVLGVFIVCWLPAF 250
Rat 201 ILLAIVALYVRIYFVVRSSHADVAGPQTLALLKTVTIVLGVFIICWLPAF 250
Human 251 SILLLDYACPVHSCPILYKAHYFFAVSTLNSLLNPVIYTWRSRDLRREVL 300
Rat 251 SILLLDSTCPVRACPVLYKAHYFFAFATLNSLLNPVIYTWRSRDLRREVL 300
Human 301 RPLQCWRPGVGVQGRRRGGTPGHHLLPLRSSSSLERGMHMPTSPTFLEGN 350
Rat 301 RPLLCWRQGKGATG.RRGGNPGHRLLPLRSSSSLERGLHMPTSPTFLEGN 349
Human 351 TVV* 353
Rat 350 TVV* 352

Figure 17B

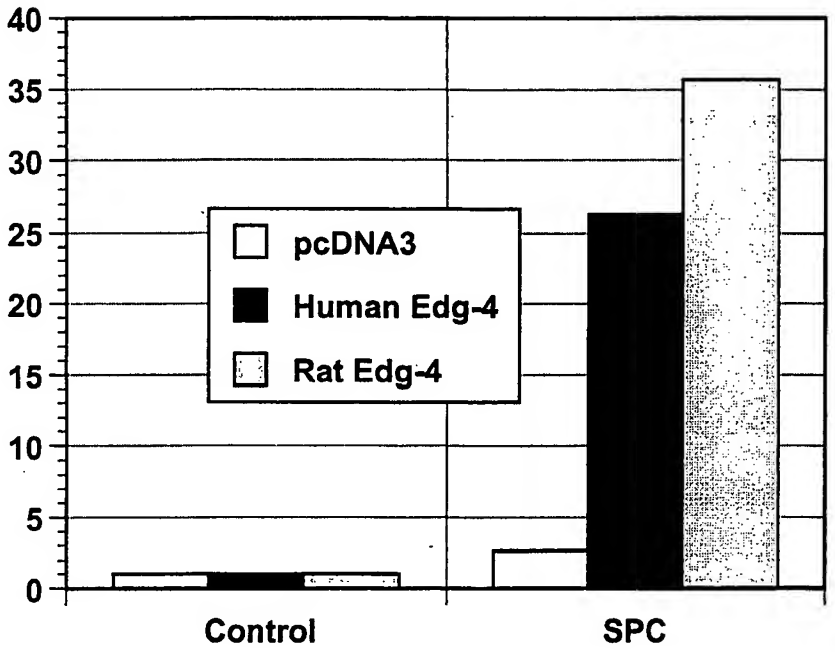
Alignment of HEDG4 with pC3-hedg4#36 translation product and rat H218 (REDG4). Differences between pC3-hedg4#36 translation product and previously determined HEDG4 polypeptide are indicated in reverse text. Differences between rat and human edg-4 polypeptide sequences are shown in bold, shaded text.

```
          1                                                    50
   HEDG4  MGSLYSEYLN PNKVQEHYNY TKETLETQET TSRQVASAFI VILCCAIVVE
HEDG4#36  MGSLYSEYLN PNKVQEHYNY TKETLETQET TSRQVASAFI VILCCAIVVE
   REDG4  MGGLYSEYLN PEKVQEHYNY TKETLDMQET PSRKVASAFI IILCCAIVVE

          51                                                   100
   HEDG4  NLLVLIAVAR NSKFHSAMYL FLGNLAASDL LAGVAFVANT LLSGSVTLRL
HEDG4#36  NLLVLIAVAR NSKFHSAMYL FLGNLAASDL LAGVAFVANT LLSGSVTLRL
   REDG4  NLLVLIAVAR NSKFHSAMYL FLGNLAASDL LAGVAFVANT LLSGPVTLSL

          101                                                  150
   HEDG4  TPVQWFAREG SAFITLSASV FSLLAIAIER HVAIAKVKLY GSDKSCRMLL
HEDG4#36  TPVQWFAREG SAFITLSASV FSLLAIAIER HVAIAKVKLY GSDKSCRMLL
   REDG4  TPLQWFAREG SAFITLSASV FSLLAIAIER QVAIAKVKLY GSDKSCRMLM

          151                                                  200
   HEDG4  LIGASWLISL VLGGLPILGW NCLGHLEACS TVLPLYAKHY VLCVVTIFSI
HEDG4#36  LIGASWLISL VLGGLPILGW NCLGHLEACS TVLPLYAKHY VLCVVTIFSI
   REDG4  LIGASWLISL ILGGLPILGW NCLDHLEACS TVLPLYAKHY VLCVVTIFSV

          201                                                  250
   HEDG4  ILLAVVALYV RIYCVVRSSH ADMAAPQTLA LLKTVTIVLG VFIVCWLPAF
HEDG4#36  ILLAVVALYV RIYCVVRSSH ADMAAPQTLA LLKTVTIVLG VFIVCWLPAF
   REDG4  ILLAIVALYV RIYFVVRSSH ADVAGPQTLA LLKTVTIVLG VFIICWLPAF

          251                                                  300
   HEDG4  SILLLDYACP VHSCPILYKA HYXFAVSTLN SLLNPVIYTW RSRDLRREVL
HEDG4#36  SILLLDYACP VHSCPILYKA HYLFAVSTLN SLLNPVIYTW RSRDLRREVL
   REDG4  SILLLDSTCP VRACPVLYKA HYFFAFATLN SLLNPVIYTW RSRDLRREVL

          301                                                  350
   HEDG4  RPLQCWRPGV GVQGRRRGGT PGHHLLPLRS SSSLERGMHM PTSPTFLEGN
HEDG4#36  RPLQCWRPGV GVQGRRRGGT PGHHLLPLRS SSSLERGMHM PTSPTFLEGN
   REDG4  RPLLCWRQGK GATGRRGGN PGHRLLPLRS SSSLERGLHM PTSPTFLEGN

          351
   HEDG4  TVV~
HEDG4#36  TVV~
   REDG4  TVV~
```

Docket No. 95-95CON

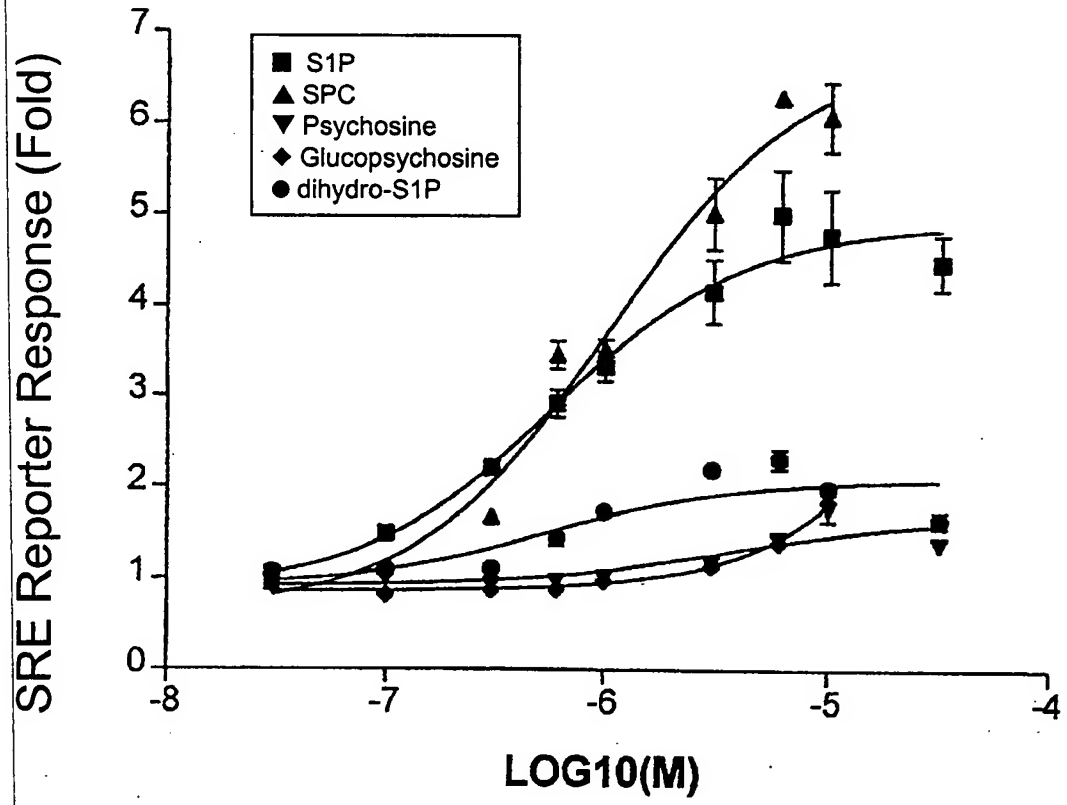
208220 "70548001

Figure 18A.



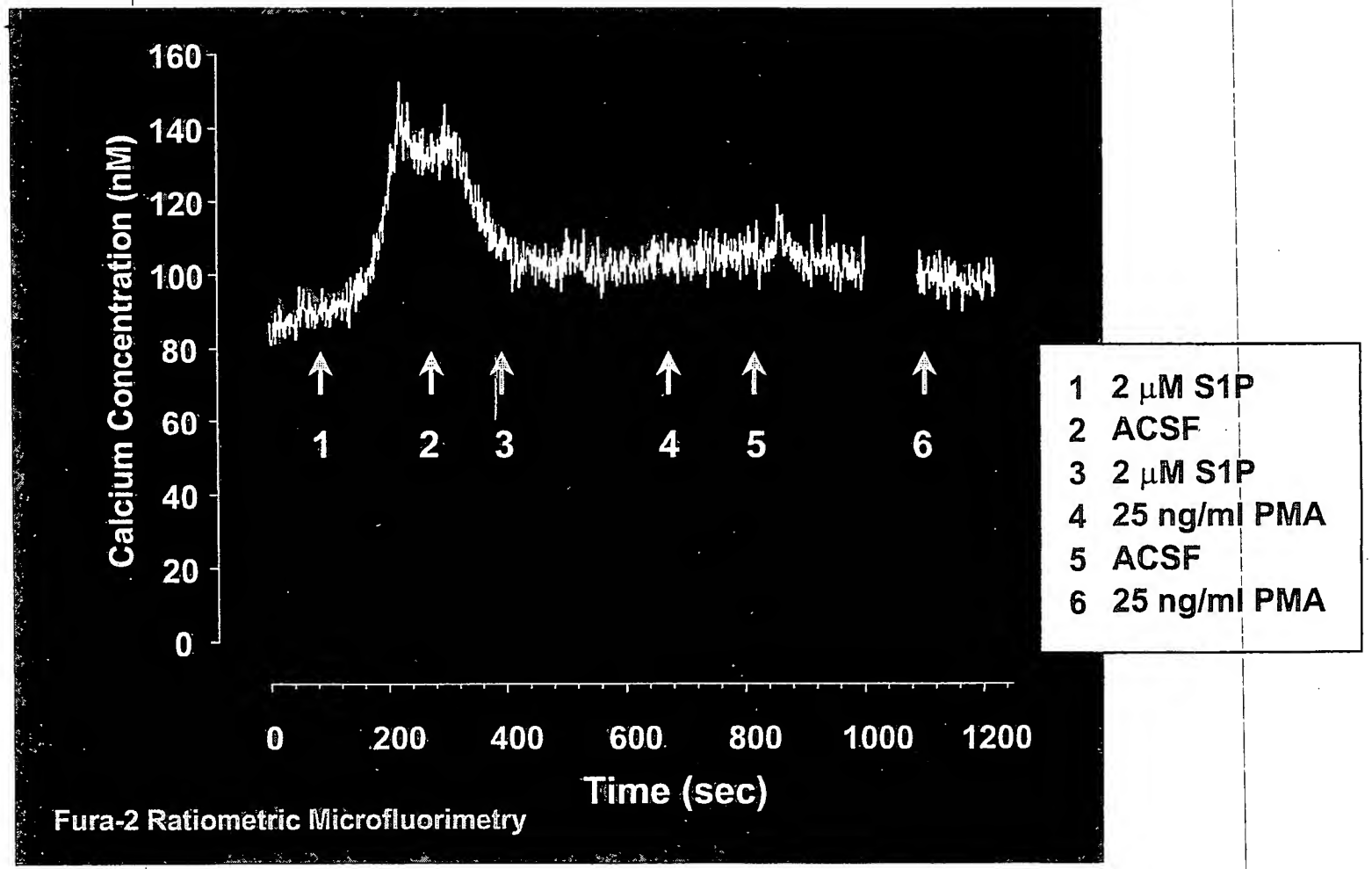
208220 "Z09h800T

Figure 18B.



208220 20Sh800T

Figure 19.



20020220 "705h800T

Figure 20.

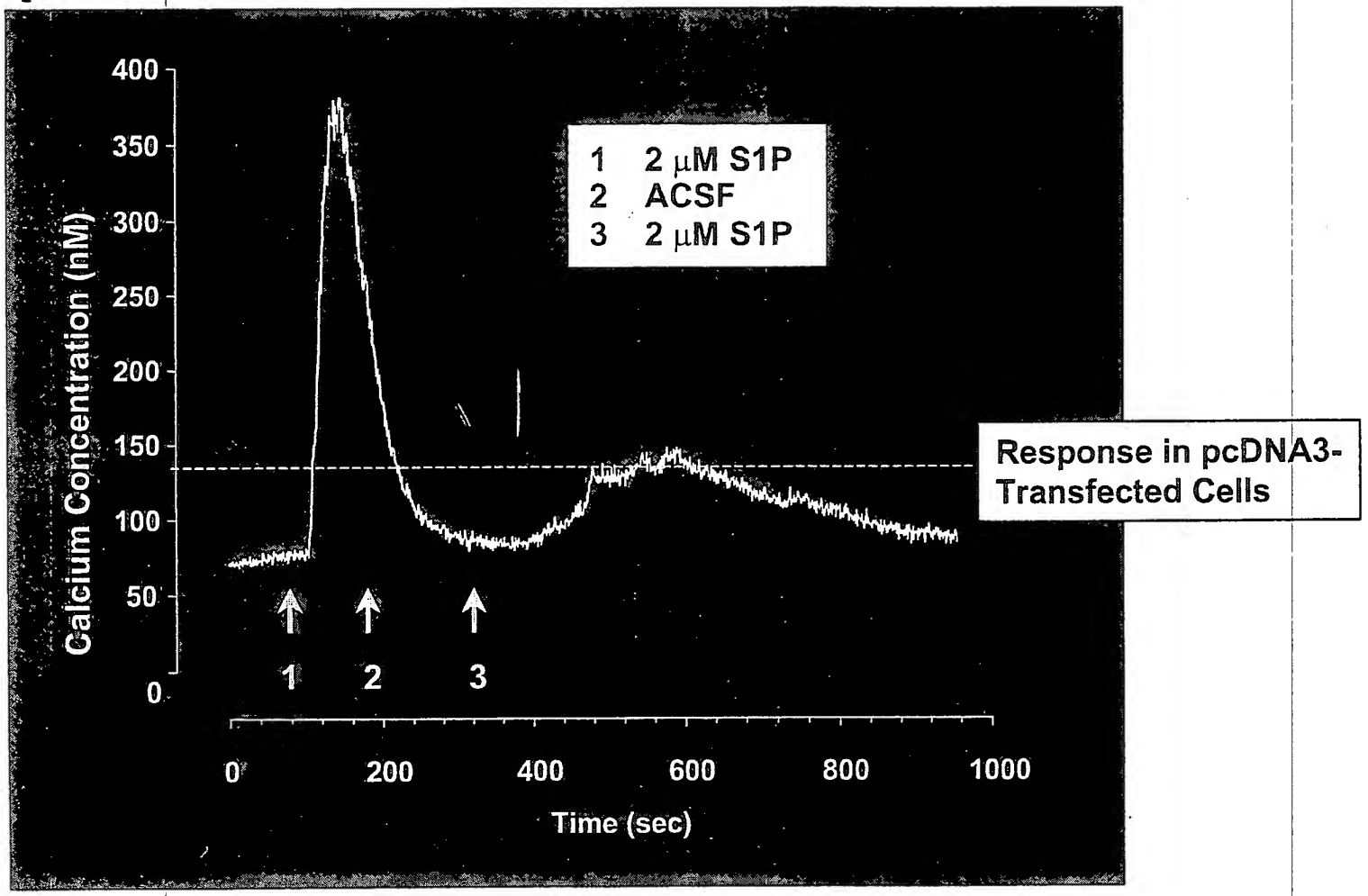


Figure 21. Human Edg-6 Amino Acid Sequence.

```
        MVIMGQCYYNETIGFFYNNSGKELSSHWRPKDVVVVALGLTVSVLVLLTNLLVIAAIASN
      1 ---------+---------+---------+---------+---------+---------+    60

        RRFHQPIYYLLGNLAAADLFAGVAYLFLMFHTGPRTARLSLEGWFLRQGLLDTSLTASVA
     61 ---------+---------+---------+---------+---------+---------+   120

        TLLAIAVERHRSVMAVQLHSRLPRGRVVMLIVGVWVAALGLGLLPAHSWHCLCALDRCSR
    121 ---------+---------+---------+---------+---------+---------+   180

        MAPLLSRSYLAVWALSSLLVFLLMVAVYTRIFFYVRRRVQRMAEHVSCHPRYRETTLSLV
    181 ---------+---------+---------+---------+---------+---------+   240

        KTVVIILGAFVVCWTPGQVVLLLDGLGCESCNVLAVEKYFLLLAEANSLVNAAVYSCRDA
    241 ---------+---------+---------+---------+---------+---------+   300

        EMRRTFRRLLCCACLRQSTRESVHYTSSAQGGASTRIMLPENGHPLMDSTL*
    301 ---------+---------+---------+---------+---------+--   352
```

10084502.020202

Figure 22. Human Edg-6 Sequence

```
          ATGGTCATCATGGGCCAGTGCTACTACAACGAGACCATCGGCTTCTTCTATAACAACAGT
        1 ---------+---------+---------+---------+---------+---------+   60
          TACCAGTAGTACCCGGTCACGATGATGTTGCTCTGGTAGCCGAAGAAGATATTGTTGTCA

          GGCAAAGAGCTCAGCTCCCACTGGCGGCCCAAGGATGTGGTCGTGGTGGCACTGGGGCTG
       61 ---------+---------+---------+---------+---------+---------+  120
          CCGTTTCTCGAGTCGAGGGTGACCGCCGGGTTCCTACACCAGCACCACCGTGACCCCGAC

          ACCGTCAGCGTGCTGGTGCTGCTGACCAATCTGCTGGTCATAGCAGCCATCGCCTCCAAC
      121 ---------+---------+---------+---------+---------+---------+  180
          TGGCAGTCGCACGACCACGACGACTGGTTAGACGACCAGTATCGTCGGTAGCGGAGGTTG

          CGCCGCTTCCACCAGCCCATCTACTACCTGCTCGGCAATCTGGCCGCGGCTGACCTCTTC
      181 ---------+---------+---------+---------+---------+---------+  240
          GCGGCGAAGGTGGTCGGGTAGATGATGGACGAGCCGTTAGACCGGCGCCGACTGGAGAAG

          GCGGGCGTGGCCTACCTCTTCCTCATGTTCCACACTGGTCCCCGCACAGCCCGACTTTCA
      241 ---------+---------+---------+---------+---------+---------+  300
          CGCCCGCACCGGATGGAGAAGGAGTACAAGGTGTGACCAGGGGCGTGTCGGGCTGAAAGT

          CTTGAGGGCTGGTTCCTGCGGCAGGGCTTGCTGGACACAAGCCTCACTGCGTCGGTGGCC
      301 ---------+---------+---------+---------+---------+---------+  360
          GAACTCCCGACCAAGGACGCCGTCCCGAACGACCTGTGTTCGGAGTGACGCAGCCACCGG

          ACACTGCTGGCCATCGCCGTGGAGCGGCACCGCAGTGTGATGGCCGTGCAGCTGCACAGC
      361 ---------+---------+---------+---------+---------+---------+  420
          TGTGACGACCGGTAGCGGCACCTCGCCGTGGCGTCACACTACCGGCACGTCGACGTGTCG

          CGCCTGCCCCGTGGCCGCGTGGTCATGCTCATTGTGGGCGTGTGGGTGGCTGCCCTGGGC
      421 ---------+---------+---------+---------+---------+---------+  480
          GCGGACGGGGCACCGGCGCACCAGTACGAGTAACACCCGCACACCCACCGACGGGACCCG

          CTGGGGCTGCTGCCTGCCCACTCCTGGCACTGCCTCTGTGCCCTGGACCGCTGCTCACGC
      481 ---------+---------+---------+---------+---------+---------+  540
          GACCCCGACGACGGACGGGTGAGGACCGTGACGGAGACACGGGACCTGGCGACGAGTGCG

          ATGGCACCCCTGCTCAGCCGCTCCTATTTGGCCGTCTGGGCTCTGTCGAGCCTGCTTGTC
      541 ---------+---------+---------+---------+---------+---------+  600
          TACCGTGGGGACGAGTCGGCGAGGATAAACCGGCAGACCCGAGACAGCTCGGACGAACAG

          TTCCTGCTCATGGTGGCTGTGTACACCCGCATTTTCTTCTACGTGCGGCGGCGAGTGCAG
      601 ---------+---------+---------+---------+---------+---------+  660
          AAGGACGAGTACCACCGACACATGTGGGCGTAAAAGAAGATGCACGCCGCCGCTCACGTC

          CGCATGGCAGAGCATGTCAGCTGCCACCCCCGCTACCGAGAGACCACGCTCAGCCTGGTC
      661 ---------+---------+---------+---------+---------+---------+  720
          GCGTACCGTCTCGTACAGTCGACGGTGGGGGCGATGGCTCTCTGGTGCGAGTCGGACCAG

          AAGACTGTTGTCATCATCCTGGGGGCGTTCGTGGTCTGCTGGACACCAGGCCAGGTGGTA
      721 ---------+---------+---------+---------+---------+---------+  780
          TTCTGACAACAGTAGTAGGACCCCCGCAAGCACCAGACGACCTGTGGTCCGGTCCACCAT

          CTGCTCCTGGATGGTTTAGGCTGTGAGTCCTGCAATGTCCTGGCTGTAGAAAAGTACTTC
      781 ---------+---------+---------+---------+---------+---------+  840
          GACGAGGACCTACCAAATCCGACACTCAGGACGTTACAGGACCGACATCTTTTCATGAAG
```

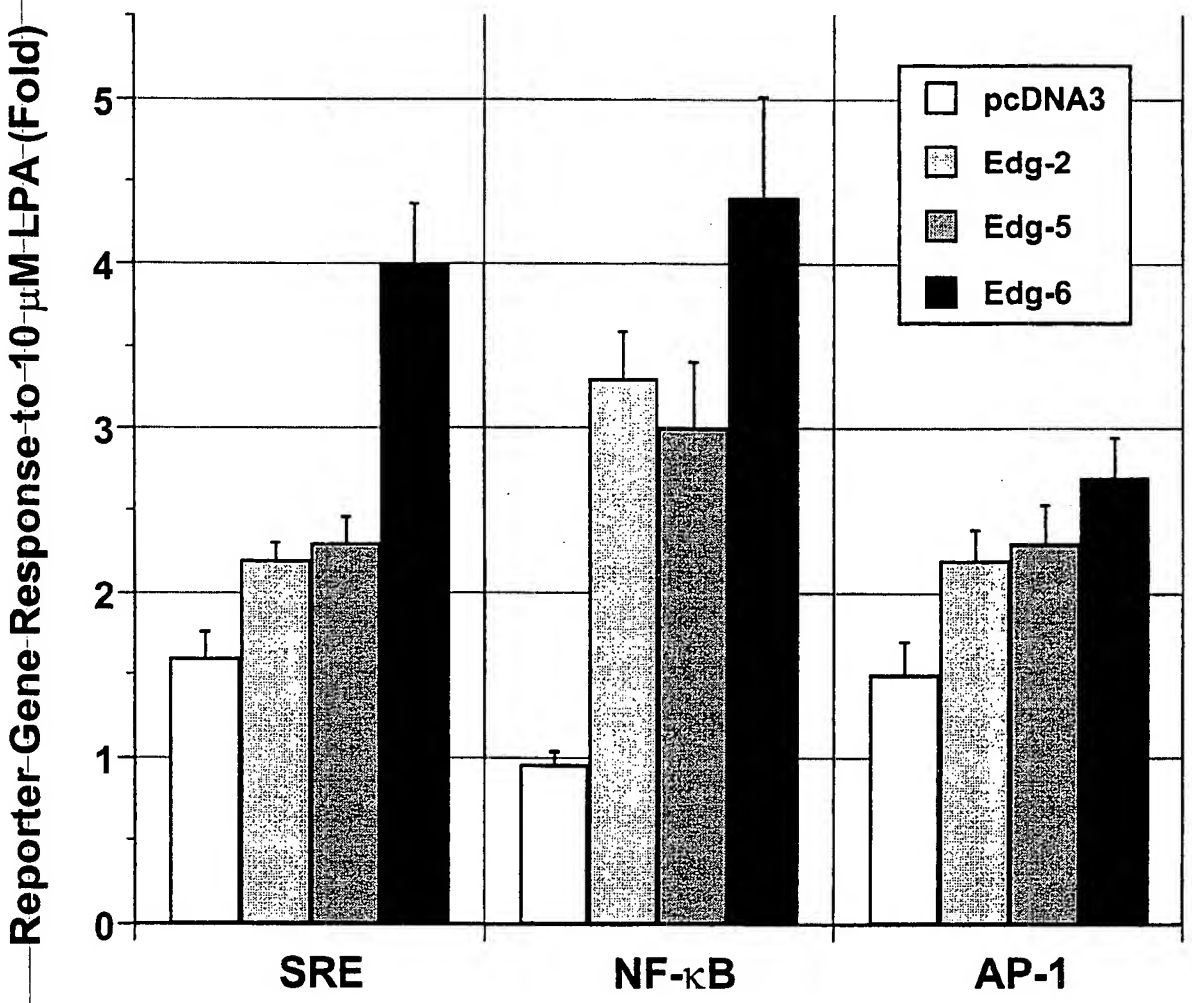
Doc#5097-0208

```
     CTACTGcTGGCCGAGGCCAACTCACTGGTCAATGCTGCTGTGTACTCTTGCCGAGATGCT
841  ---------+---------+---------+---------+---------+---------+  900
     GATGACgACCGGCTCCGGTTGAGTGACCAGTTACGACGACACATGAGAACGGCTCTACGA

     GAGATGCGCCGCACCTTCCGCCGCCTTCTCTGCTGCGCGTGCCTCCGCCAGTCCACCCGC
901  ---------+---------+---------+---------+---------+---------+  960
     CTCTACGCGGCGTGGAAGGCGGCGGAAGAGACGACGCGCACGGAGGCGGTCAGGTGGGCG

     GAGTCTGTCCACTATACATCCTCTGCCCAGGGAGGTGCCAGCACTCGCATCATGCTTCCC
961  ---------+---------+---------+---------+---------+---------+ 1020
     CTCAGACAGGTGATATGTAGGAGACGGGTCCCTCCACGGTCGTGAGCGTAGTACGAAGGG

     GAGAACGGCCACCCACTGATGGACTCCACCCTTTAG
1021 ---------+---------+---------+------  1056
     CTCTTGCCGGTGGGTGACTACCTGAGGTGGGAAATC
```

EP 0 845 007 B1

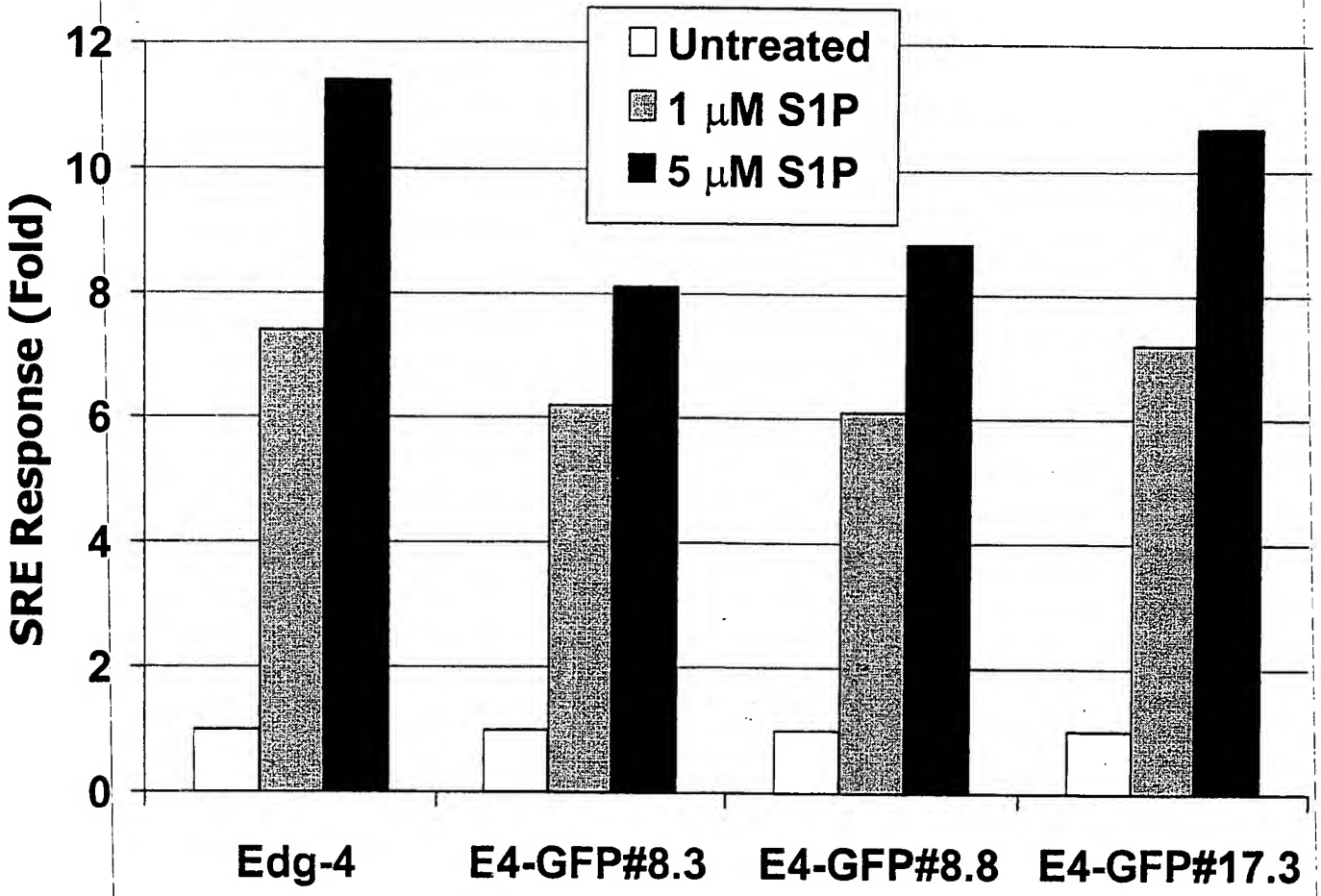
208220 "ZOSHBOOT

Figure 23.



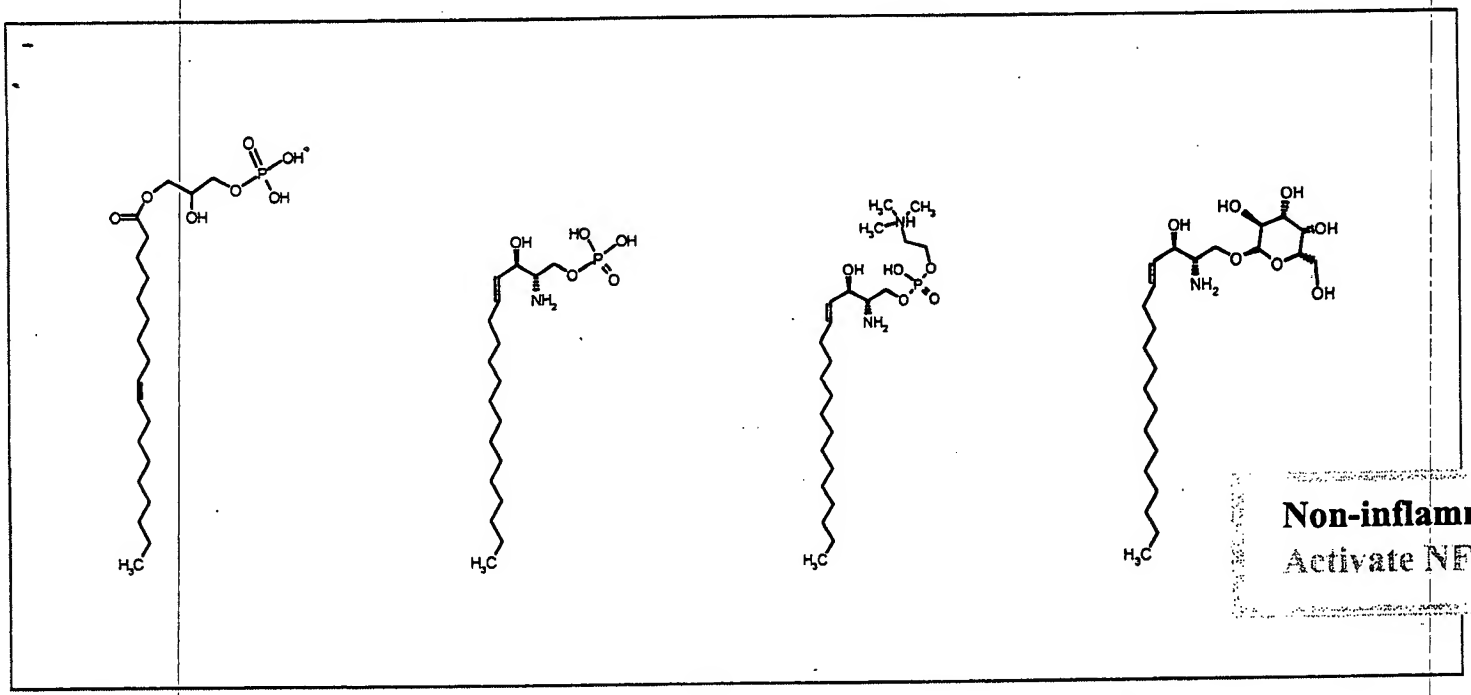
208220" 20sh800F

Figure 24.



20822D" 205h80DT

Figure 25.



LPA	S1P	SPC	Psychosine
Edg-2	**Edg-1**	**Edg-1**	Edg-3
Edg-5	Edg-3	Edg-3	Edg-4
Edg-6	Edg-4	Edg-4	
	Edg-7	**Edg-7**	